Unsymmetrical Ketone Synthesis via a Three-Component Connection Reaction of Organozincs, Allylating Agents, and Carbon Monoxide

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A wide variety of organozincs (diethylzinc, alkylzinc halides, and organozincs **2**, **5**, and **9a–e**, functionalized with ester and nitrile groups) undergo a three-component connection reaction with carbon monoxide and allylic benzoates or phosphates **1a–h** to furnish unsymmetrical ketones, e.g., **3**, **6**, and **10**, in good yields under 1 atm of carbon monoxide at ambient temperature by the catalysis of tetrakis(triphenylphosphine)palladium in THF/HMPA. The regio- and stereoselectivities of the present carbonylation show marked contrast to those reported for the palladium-catalyzed carbonylation of unsymmetrical allylic substrates. For example, the reaction of crotyl benzoate with octylzinc iodide provides all the possible stereo- and regioisomers, i.e., *cis*- and *trans*-2-butenyl and 1-methyl-2-propenyl octyl ketones in comparable amounts. The carbonylative coupling of carvyl phosphates, *trans*- and *cis*-**1h**, and γ-zincio ester **5** is stereospecific and proceeds with inversion of configuration at the allylic stereocenters to furnish *cis*- and *trans*-**6h**, respectively, as single diastereomers. In the absence of HMPA, the reaction feature changes dramatically and lactones **12** and **13** (composed of organozincs, carbon monoxide, and allylating agents in the ratios of 1:1:2 and 2:1:1, respectively) and symmetrical keto diesters **14** (composed of 2 mol of organozincs and 1 mol of carbon monoxide) are formed in varying ratios depending on the reaction conditions. Synthetic scope of the unsymmetrical ketones and mechanistic rationale for these unique and unprecedented reaction behaviors are discussed.

Introduction

Direct use of carbon monoxide as the component of carbonyl groups of aldehydes, ketones, carboxylic acids, and their derivatives is very important from practical point of view. Accordingly, extensive studies have been done in pursuit of the development of efficient carbonylation processes, examining a variety of transition metal catalysts.[1] Compared with the synthesis of aldehydes and carboxylic acid derivatives, however, only a limited number of methods for the synthesis of ketones under carbonylation conditions have been described, probably reflecting the difficulties associated with this process. Concurrently, owing to the importance of ketones as the final products as well as the synthetic intermediates, the chemistry based on the idea of "carbon monoxide equivalents" has been developed in a last few decades.[2]

Ketone synthesis via carbonylation reactions may be promoted or catalyzed by transition metals, such as Pd,[3] Fe,[4] Co,[5] Ni,[6] Cu,[7] Ru,[8] Ti,[9] and Zr,[10] in most cases under high pressures of carbon monoxide. Among these, the methods developed by Tanaka[3i] and Stille[3c,d,f–h] may be the most efficient and versatile, since organotin reagents, one of the reaction partners, tolerate many functional groups and undergo carbonylative coupling reaction with a variety type of electrophiles (e.g., allyl halides, aromatic and vinylic halides and triflates) by the catalysis of palladium complexes under pressures of carbon monoxide (about 30 atm).

Almost 10 years ago, we also demonstrated that palladium complexes nicely catalyze the coupling reaction of alkylzinc iodides and aromatic iodides to give alkyl aryl ketones in good yields.[11] The outstanding feature of this

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reaction is that it can be performed under an atmospheric pressure of carbon monoxide (a balloon). In the meantime, we have also shown that organozincs having many electrophilic functionalities of synthetic importance, such as ester, amide, nitrile, ketone, and halide, can be prepared in good yields and in high reproducibility in millimole to mole scales, and they undergo various types of carbon–carbon bond formation reactions in the presence of appropriate catalysts and/or promoters.[12]

In this paper, we describe that organozincs (diethylzinc, octylzinc halides, and organozincs **2**, **5**, and **9a–e**, functionalized with ester and nitrile groups) undergo a three-component connection reaction with carbon monoxide and a variety of allylating agents **1a–h** to furnish unsymmetrical ketones, e.g., **3**, **6**, and **10**, in good yields *under very mild conditions, 1 atm of carbon monoxide and room temperature*, by the catalysis of tetrakis(triphenylphosphine)palladium (eqs 1–3).

The reaction mechanism of the present reaction seems to be quite different from those reported for the palladium-catalyzed carbonylation reactions of allylic substrates. Generally, palladium(0)-catalyzed carbonylation of crotyl type substrates is known to provide *trans*-2-butenylcarbonyl derivatives selectively.[13] In the present reaction, however, all the possible stereo- and regioisomers, i.e., *cis*- and *trans*-2-butenyl and 1-methyl-2-propenyl ketones, are obtained (e.g., Table 5). The ratio of regioisomers (2-butenyl to 1-methyl-2-propenyl) depends on the electronic nature of the organic moieties of organozinc reagents; the stronger the electron-donating ability of the organic moieties, the higher the proportion of 1-methyl-2-propenyl ketone isomers. Furthermore, only a slight change in the reaction conditions causes dramatic alteration in the reaction course, and lactones **12** and **13** (composed of organozincs, carbon monoxide, and allylating agents in the ratios of 1:1:2 and 2:1:1, respectively) and symmetrical keto diesters **14** (composed of 2 mol of organozincs and 1 mol of carbon monoxide) are formed exclusively or predominantly over the unsymmetrical ketones (eqs 4–6). The synthetic scope of unsymmetrical ketones and these unique and unprecedented reaction behaviors as well as a mechanistic rationale for these observations are presented here. A part of the present work was reported as a communication.[14]

Results and Discussion

A variety of organozinc reagents **2**, **5**, and **9a–e** (Figure 1) that have electrophilic functional groups and octylzinc iodide can be prepared in quantitative yields by the reaction of the corresponding iodides with a slight excess amount of zinc–copper couple in the presence of 1.5 equiv

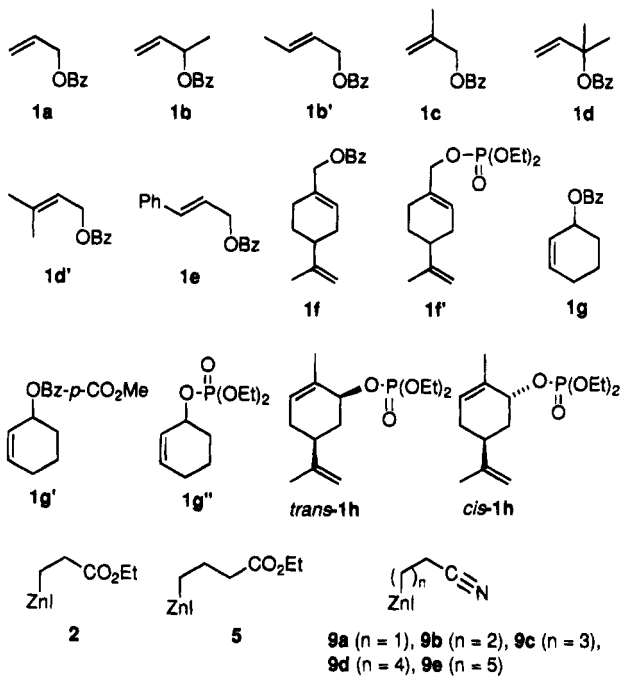
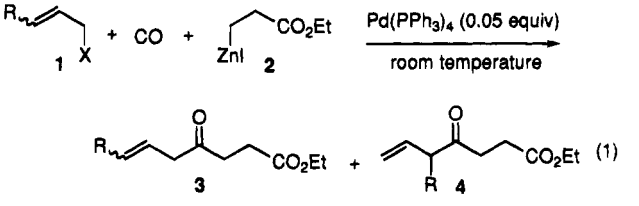


Figure 1. Structures of allylating agents **1** and organozincs **2**, **5**, and **9**.

of hexamethylphosphoric triamide (HMPA) or *N,N*-dimethylacetamide (DMA). In order to generate these organozincs in good yields and with high reproducibility, these aprotic dipolar solvents are indispensable. Ethyl β-iodopropionate is so reactive that β-zincio ester **2** may be generated in a good yield by the zincation of this iodide in the absence of these cosolvents.

Three-Component Connection Reaction with β-Zinciopropionate 2. β-Zincio ester **2**, prepared *in situ*, undergoes a smooth carbonylative coupling reaction with allylic benzoates **1** to give unsymmetrical ketones **3**, composed of **2**, carbon monoxide, and an allylating agent **1** in a ratio of 1:1:1, by the catalysis of tetrakis(triphenylphosphine)palladium under atmospheric pressure of carbon monoxide and at ambient temperature (eq 1). Results are summarized in Table 1.



For the carbonylation to proceed successfully, the use of HMPA is essential. Interestingly, as summarized in Table 2, the yields of **3a** markedly depend on the amount of HMPA. Being maximal with 11.3 equiv of HMPA, relative to allyl benzoate **1a**, with the larger and especially with the smaller amounts of HMPA, the yields of **3a** fall off sharply. *In the absence of HMPA, **3a** was not formed in any detectable amounts* (run 1, Table 2). Accordingly, all the reactions of β-zincio esters with allylic benzoates **1a–d** were undertaken in the presence of 11.3 equiv of HMPA.

As being general for the palladium-catalyzed carbonylation of unsymmetrically substituted allylic substrates,[13] both α-methylallyl benzoate (**1b**, run 2, Table 1) and crotyl benzoate (**1b'**, run 3, Table 1) selectively provided the same ketone **3b** with the least number of substituents

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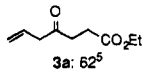
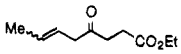
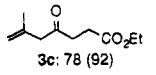
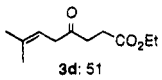
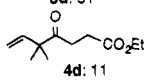
Table 1. Pd⁰-Catalyzed Three-Component Connection Reaction with β-Zincio Esters 2[1]

run	allylating agent	equiv[2] of 2	solv/additive(s) (equiv)[2,3]	time (h)	% isolated yields of products 3 and 4 (% conversion)[4]
1	1a	2.5	THF/HMPA (11.3)	18	 3a: 62[5]
2	1b	2.5	THF/HMPA (11.3)	23	 3b: 67 (*cis*:*trans* = 31:69)
3	1b'	2.5	THF/HMPA (11.3)	69	3b: 52
4	1c	2.5	THF/HMPA (11.3)	26	 3c: 78 (92)
5	1d	2.5	THF/HMPA (11.3)	24	 3d: 51  4d: 11

[1] For the structures of allylating agents **1** and organozincs **2**, see Figure 1. [2] Equivalencies are meant to refer to the amounts of the reagents relative to allylating agents **1**. [3] Reactions were performed under the following conditions: **1** (1 mmol), **2** (2.5 mmol, generated *in situ* from 2.5 mmol of ethyl β-iodopropionate and zinc–copper couple in 5 mL of THF in the presence of 11.3 mmol of HMPA), and $Pd(PPh_3)_4$ (0.05 mmol) at room temperature under CO (1 atm, a balloon). THF, tetrahydrofuran; HMPA, hexamethylphosphoric triammide. [4] Unless otherwise specified, conversion is 100%. Yields are for the isolated, spectroscopically homogeneous products, based on the conversion of **1**. [5] In addition to **3a**, diethyl 4-oxopimelate (**14a**) was isolated in 12% yield (see the first column, Scheme 5).

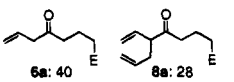
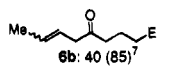
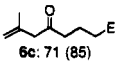
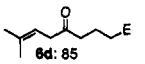
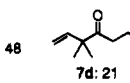
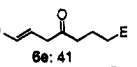
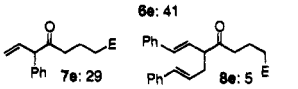
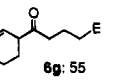
Table 2. Effects of the Amounts of HMPA on the Yields of 3a for the Three-Component Connection Reaction of β-Zincio Ester 2, Allyl Benzoate 1a, and Carbon Momoxide[1]

run	equiv of HMPA[2]	reaction time (h)	% conversion[3]	% isolated yield of 3a[4,5]
1	0.0	48	100	0[6]
2	3.7	50	40	5
3	7.5	50	94	33
4	11.3	18	100	62[7]
5	15.0	17	100	49
6	22.5	17	100	33

[1] Reactions were performed under the following conditions: allyl benzoate (**1a**, 1 mmol), β-zinciio ester (**2**, 2.5 mmol), and $Pd(PPh_3)_4$ (0.05 mmol) in THF (5 mL) under 1 atm of carbon monoxide (a balloon) at room temperature. [2] β-Zincio ester (**2**), free from HMPA, was prepared in situ from 2.5 mmol of ethyl β-iodopropionate and zinc–copper couple in 5 mL of THF, and then the indicated amount of HMPA relative to **1a** was added to the mixture. [3] Conversions are based on **1a**. [4] Yields refer to the isolated, spectroscopically homogeneous **3a**. [5] In runs 3–6, in addition to **3a**, was obtained **14a** in ca. 10% yield. [6] The products obtained in this reaction are γ-allyl-γ-(β-ethoxycarbonylethyl)-γ-butyrolactone (**13a**, 59%), diethyl 4-oxopimelate (**14a**, 21%), γ,γ-diallyl-γ-butyrolactone (**12a**, 9%) (see eq 4). [7] In addition to **3a**, diethyl 4-oxopimelate (**14a**) was obtained in 12% yield (see the first column, Scheme 5).

at the carbon α to the carbonyl group. Surprisingly, however, the ketone **3b** was isolated as a mixture of *cis* and *trans* isomers in a ratio of ca. 1:2. Moreover, the reaction with α,α-dimethylallyl benozate (**1d**) provided an unexpected regioisomeric ketone, α,α-dimethylallyl ketone **4d**, as a minor product together with γ,γ-dimethylallyl ketone **3d** (run 5, Table 1). These stereo- and regiochemical anomalies will be discussed later in the section Three-Component Connection Reaction with Zincio Nitriles **9**.

Table 3. Pd⁰-Catalyzed Three-Component Connection Reaction with γ-Zincio Ester 5[1]

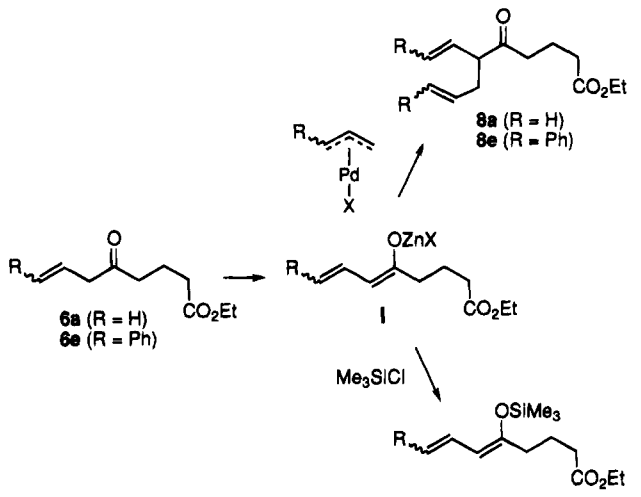
run	allylating agent	equiv[2] of 5	solv/additive(s) (equiv)[2,3]	time (h)	% isolated yields of products, 6, 7, and 8 (% conversion)[4,5]
1	1a	1.5	toluene/HMPA (2.3)	30	 6a: 40 8a: 28
2	1a	3.0	THF/HMPA (4.5)	30	6a: 43, 8a: 26
3	1a	3.0	THF/HMPA (4.5)/TMSCl (4.0)[6]	30	6a: 78
4	1b	1.5	toluene/HMPA (2.3)	24	 6b: 40 (85)[7]
5	1b'	1.5	toluene/HMPA (2.3)	14	6b: 85 (71)[7]
6	1c	1.5	toluene/HMPA (2.3)	24	 6c: 71 (85)
7	1d	1.5	toluene/HMPA (2.3)	24	 6d: 85
8	1d	2.5	toluene/HMPA (11.3)	24	 6d: 48 7d: 21
9	1d'	1.5	toluene/DMA (2.3)	24[8]	6d: 60
10	1e	3.0	THF/HMPA (4.5)	22	 6e: 41  7e: 29 8e: 5
11	1e	3.0	THF/HMPA (4.5)/ TMSCl (4.0)	40	6e: 64
12	1e	3.0	THF/DMA (4.5)/ TMSCl (4.0)	20	6e: 74
13[9]	1g'	3.0	THF/HMPA (11.3)	48	 6g: 55
14	1g''	3.0	THF/HMPA (11.3)	23	6g: 57

[1] For the structures of allylating agents **1** and γ-zincio ester **5**, see Figure 1. [2] Equivalencies are meant to refer to the amounts of the reagents relative to allylating agents **1**. [3] Unless otherwise specified, reactions were performed under the following conditions: **1** (1 mmol), **5** (generated *in situ* from the indicated amount of ethyl γ-iodobutyrate and zinc–copper coouple in the presence of the indicated amount of HMPA or DMA in 5 mL of a given solvent), and $Pd(PPh_3)_4$ (0.05 mmol) at room temperature under CO (1 atm, a balloon). HMPA, hexamethylphosphoric triamide; DMA, *N*,*N*-dimethylacetamide; TMSCl, chlorotrimethylsilane. [4] The symbol E stands for ethoxycarbonyl group. [5] Unless otherwise specified, conversion is 100%. Yields are for the isolated, spectroscopically homogeneous products, based on the conversion of **1**. [6] The same reaction in toluene/HMPA (4.5 equiv)/chlorotrimethylsilane (4.0 equiv) was heterogeneous and provided a complex mixture of products. [7] The isomer ratio (*cis*:*trans*) was not determined. [8] The reaction was carried out at 40 °C. [9] The similar reaction using **1g**, in place of **1g'**, was very slow and gave **6g** in 28% isolated yield (53% conversion based on **1g**) after 69 h at room temperature.

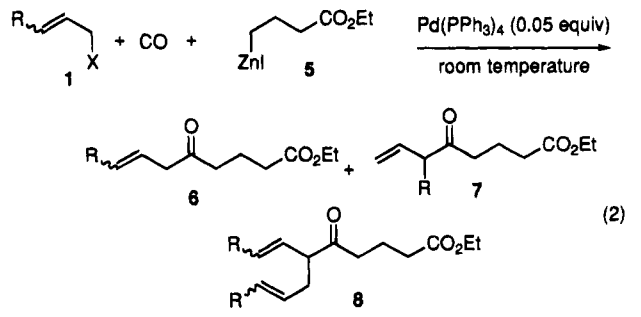
The reaction of **2** with γ,γ-dimethylallyl benzoate (**1d'**) was unsuccessful under the similar and somewhat modified conditions (either at the higher or lower temperatures, with increased amounts of **2**). All these reactions with **1d'** were very slow, and the formation of **3d** and/or **4d** could not be confirmed owing to the complexity of the reaction mixtures (VPC and ^1H NMR).

Three-Component Connection Reaction with γ-Zincio Ester 5. In Table 3 are summarized the results of the three-component connection reaction of γ-zincio ester **5**, carbon monoxide, and allylating agents **1** (eq 2). As apparent from this table, the reaction is quite general for allylating agents with a wide structural variety and proceeds smoothly at room temperature under 1 atm of carbon monoxide by the catalysis of 5 mol % of Pd⁰

Scheme 1



species. Toluene and THF can be used as the solvent in similar efficiency. HMPA is indispensable as a cosolvent. Although examined for only the limited number of reactions, *N,N*-dimethylacetamide (DMA) seems to work similarly well as a cosolvent (run 9).



(2)

γ-Zincio ester **5** displays apparently different reactivity from β-zincio ester **2** in many respects. The carbonylative coupling reaction of **5** is not affected by the amounts of HMPA as much as the reaction of **2**. Unsymmetrical ketones **6**–**8** were obtained in satisfactory yields with varying amounts of HMPA, ranging from 2.3 equiv (e.g., runs 1 and 4–7, Table 3) to 11.3 equiv (e.g., runs 13 and 14).

The most striking difference between the reactions with β- and γ-zincio esters is the formation of the doubly allylated products **8** with the latter (eq 2). The products **8**, being produced only for the reactions with allyl benzoate (**1a**, runs 1 and 2) and cinnamyl benzoate (**1e**, run 10, Table 3) among many other allylating agents examined, were first expected to be derived by an allylation of zinc dienolates **I** with π-allylpalladium (Scheme 1), the former being generated by the deprotonation of the primary products **6** with γ-zincio ester at the most acidic methylene protons flanked with ketocarbonyl and olefinic double bond, since not only may those protons in **6a** and **6e** under consideration be more acidic and sterically more accessible (for **6a**) than the corresponding protons of the other derivatives of **6**, but also γ-zincio ester is apparently more basic than β-zincio ester.

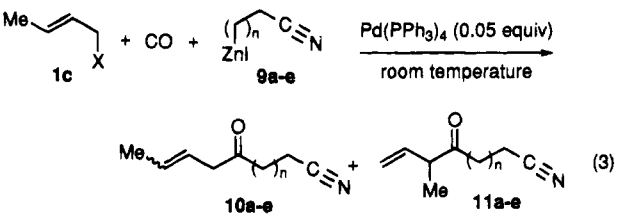
With this idea in mind, we examined the reactions of **5** with **1a** and **1e** in the presence of 4 equiv of chlorotrimethylsilane, relative to benzoate, in anticipation of the faster trapping the dienoates **I** with chlorosilane as their dienyl silyl ethers than with π-allylpalladium and recovering **6** after hydrolysis of the dienyl silyl ethers. This idea seemed to have worked well, since under such conditions **6a** (run 3) and **6e** (runs 11 and 12, Table 3) were obtained selectively and in good yields, seemingly at the expense of **8a** and **8e**, respectively. However, neither the D_2O quenching of the reaction mixture of run 3 (Table 3) nor the D_2O treatment of the mixture obtained by exposing the isolated **6a** to 2 equiv of γ-zincio ester (at room temperature for 24 h) introduced any detectable amounts of deuterium at the allylic position of **6a**. Although we are unable to delineate the reaction mechanism responsible for the formation of **8** and the real role that chlorotrimethylsilane plays, the use of chlorotrimethylsilane is beneficial for the high yield and selective formation of **6** for those cases where **8** contaminates the reactions.

Among allylic benzoates, 2-cyclohexenyl benzoate (**1g**, run 13, footnote 9, Table 3) was exceptionally reluctant toward carbonylation and almost the half of the starting benzoate was recovered under the usual reaction conditions. *p*-(Methoxycarbonyl)benzoate (**1g′**, run 13) and diethyl phosphate (**1g″**, run 14, Table 3) turned out to be more reactive and provided the same ketone **6g** in almost the same yields. *p*-Nitrobenzoate was more reactive and attained completion within 16 h under the similar reaction conditions, however, provided **6g** in a lower yield (38%).

The regioselectivity for the reaction of **5** with unsymmetrically substituted allylating agents is as usual, and the terminally substituted β,γ-unsaturated ketones are obtained selectively, i.e., **6b** from **1b** and **1b′** (runs 4 and 5) and **6d** from **1d** and **1d′** (runs 7 and 9, Table 3). A mechanistic rationale for the formation of the regioisomeric product **7d**, observed for the reaction undertaken in the presence of a larger amount of HMPA (run 8, Table 3), will be given in the following two sections.

The reaction behavior of cinnamyl benzoate (**1e**) is apparently different from other allylic benzoates. For the reaction with β-zincio ester **2**, despite our extensive experimentations applying the usual and somewhat modified conditions, **1e** did not provide the expected ketone. For the reaction with γ-zincio ester **5**, on the other hand, it furnished the unusual α-substituted product **7e** in a comparable amount to the normal γ-substituted product **6e** (run 10, Table 3; see also run 4, Table 5).

Three-Component Connection Reaction with Zincio Nitriles 9a–e: Regioselectivity for the Reactions with Crotyl Benzoate. In order to clarify the origin of the hitherto sporadically observed unusual regioselectivity (providing α-substituted ketones **4** and **7**), the carbonylative coupling reaction was examined in detail using crotyl benzoate as a representative of unsymmetrical allylic benzoates and zincio nitriles **9** with various lengths of carbon chain connecting zinc and nitrile group (eq 3). Results are summarized in Table 4.



(3)

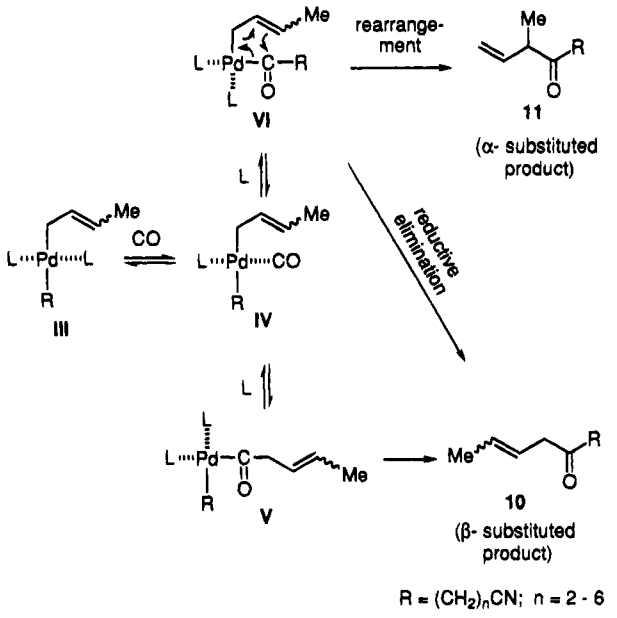
With β- (**9a**) and γ-zincio nitriles (**9b**), only the γ-substituted products **10a** and **10b**, respectively, were obtained as with the cases of β- and γ-zincio esters (run 2, Table 1, and runs 4 and 5, Table 3). Interestingly, however,

Table 4. Pd-Catalyzed Three-Component Connection Reaction of Crotyl Benzoate (1b'), Carbon Monoxide, and Zincio Nitriles 9a–e[1]

run	zincionitrile	time[2] (h)	% conversion[3]	% isolated yield[4] 10	% isolated yield[4] 11	product ratio 10:11
1	**9a** (n = 1)	48	100	**10a** (n = 1): 33	**11a** (n = 1): 0	100:0
2	**9b** (n = 2)	29	100	**10b** (n = 2): 67[5]	**11b** (n = 2): 0	100:0
3	**9c** (n = 3)	29	84	**10c** (n = 3): 32	**11c** (n = 3): 11	74:26
4	**9d** (n = 4)	34	100	**10d** (n = 4): 45[6]	**11d** (n = 4): 25	64:36
5	**9e** (n = 5)	20	100	**10e** (n = 5): 44[7]	**11e** (n = 5): 40	52:48

[1] For the structures of **9a–e**, **10a–e**, and **11a–e**, see Figure 1 and eq 3. [2] Reactions were undertaken under the following conditions: crotyl benzoate (**1b'**, 1 mmol), zincionitrile (**9a–e**, 2.5 mmol, generated *in situ* from the corresponding iodonitrile (2.5 mmol) and zinc–copper couple in 5 mL of THF containing 11.3 mmol of HMPA), and $Pd(PPh_3)_4$ (0.05 mmol) under 1 atm of CO (a balloon) at room temperature. [3] Conversion is based on **1b'**. [4] Yields refer to the isolated yields of spectroscopically homogeneous **10a–e** and **11c–e**, based on conversion of **1b'**. [5] **10b** was isolated as a mixture of *cis* and *trans* isomers (*cis*:*trans* = 28:72). [6] **10d** was isolated as a mixture of *cis* and *trans* isomers (*cis*:*trans* = 28:72). [7] **10e** was isolated as a mixture of *cis* and *trans* isomers (*cis*:*trans* = 36:64).

Scheme 2. Rationale for Unusual Regio- and Stereoselectivity Observed for the Three-Component Connection Reactions of Zincio Nitriles 9a–e, Crotyl Benzoate (1c), and Carbon Monoxide



with an increase in the number of the methylene unit, the amounts of the α-substituted products **11** increased gradually. And finally, the reaction with ζ-zincio nitrile **9e** (run 5, Table 4) provided both the α- and γ-substituted products almost in the equal amounts. Furthermore, careful examinations of the γ-substituted products **10** by means of high-field ^1H NMR revealed that these ketones are composed of the *cis* and *trans* isomers in a ratio of ca. 1:2.

These regiochemical (providing α-substituted products) and stereochemical (providing *cis* isomers) outcomes are quite unexpected. A host number of precedents have shown that the palladium-catalyzed carbonylation of crotyl and α-methallyl substrates provides *trans*-2-butenylcarbonyl isomers in high regio- and stereoselectivity.[13]

A rationale for the striking regiochemical and stereochemical anomalies observed for the reactions with δ-, ϵ-, and ζ-zincio nitriles is outlined in Scheme 2, which supposes an intermediacy of σ-allylalkylpalladium complex **III** and its carbonylated derivative **IV** as the key intermediates (*vide infra*). Through **IV**, a competitive migratory insertion of the σ-allyl and (ω-cyano)alkyl groups to carbonyl might take place. Although the relative migratory aptitude among alkyl groups toward insertion to carbon monoxide in dialkylcarbonylpalladium complexes is not defined yet, we assume, as an extrapolation of well-studied manganese case,[15] that electron-donating groups undergo migratory insertion faster than electron-withdrawing groups. Accordingly, when R is electron attracting, as β- and γ-zincio esters and nitriles, σ-allyl groups may selectively undergo migratory insertion to carbon monoxide to give an acylpalladium intermediate **V**, which further undergoes a reductive elimination to provide the γ-product **10**. Production of **10** as a mixture of *cis* and *trans* isomers seems to reflect that a σ-allyl rather than π-allylpalladium species is responsible for the carbonylation and that the σ-crotylpalladium complex **IV** exists as a mixture of *cis* and *trans* isomers that equilibrate with each other via a σ-(1-methyl)-allylpalladium intermediate.

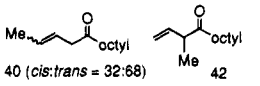
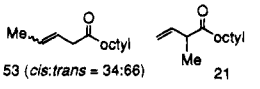
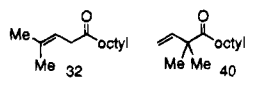
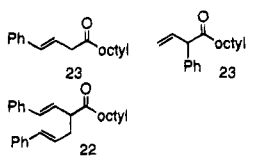
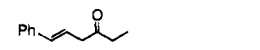
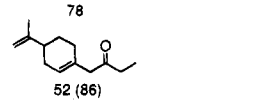
When R is electron releasing, as δ-, ϵ-, and ζ-zincio nitriles, on the other hand, the carbonylation of these groups may well compete with the carbonylation of σ-allyl groups and provides **VI** in substantial proportion. The thus-formed **VI** is assembled ideally for six-electron migration (indicated with three curved arrows) and might undergo a rearrangement (either sigmatropic or ionic) to give the unusual α-substituted isomer **11**. Through **VI**, reductive elimination to give **10** may occur concurrently.

Three-Component Connection Reaction with Octylzinc Iodide and Diethylzinc. In order to appraise the mechanism proposed in Scheme 2, we examined the regio- and stereochemical outcomes for the reactions of octylzinc iodide with unsymmetrical allylating agents in an expectation that octylzinc iodide, being the most electron releasing among organozincs discussed hitherto, should provide the α-substituted products in the highest proportion. Indeed, this provides to be the case (runs 1–4, Table 5), and for the first time the yields of the α-substituted products exceeded those of the γ-substituted products for the reactions with crotyl (run 1) and α,α-dimethylallyl benzoates (run 3, Table 5). As having been observed for the reactions with β- and γ-zincio esters, cinnamyl benzoate displayed unusual reactivity also toward the reaction with octylzinc iodide and provided three kinds of ketones with *all-trans* stereochemistry in comparable amounts (*trans*-cinnamyl, α-phenylallyl, and *trans*-1-(*trans*-β-styryl)-4-phenyl-3-butenyl octyl ketones, run 4, Table 5). Crotyl benzoate provided the γ-substituted product as a mixture of *cis* and *trans* isomers in a ratio of ca. 1:2 (run 1, Table 5).

These results clearly indicate that the unusual regio- and stereochemical outcomes are not brought about from some special interactions (e.g., inter- and intramolecular

(15) (a) Collman, J. P.; Hegedus, L. S. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, California, 1980; Chapter 5.1. (b) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*; Wiley; New York, 1988; Chapter 7.2.

Table 5. Pd^0-Catalyzed Three-Component Connection Reaction with Nonfunctionalized Organozincs, Octylzinc Iodide, and Diethylzinc

run	allylating agent[1]	organozinc[2,3]	solv/additive(s) (equiv)[4]	temp. (°C), time (h)	% isolated yields of products (% conversion)[5]
1	**1b'**	*n*-octylZnI	THF/HMPA (11.3)	r.t., 26	 40 (*cis*:*trans* = 32:68) 42
2	**1b'**	*n*-octylZnI	THF/HMPA (3.8)	r.t., 22	 53 (*cis*:*trans* = 34:66) 21
3	**1d**	*n*-octylZnI	THF/HMPA (11.3)	r.t., 28	 32 40
4	**1e**	*n*-octylZnI	THF/HMPA (11.3)	r.t., 26	 23 23 22
5	**1e**	Et_2Zn	toluene-hexane	0, 24	 78
6	**1f'**[6]	Et_2Zn	toluene-THF	0, 70	 52 (86)
7	**1f'**[6]	Et_2Zn	THF/HMPA (11.3)	r.t., 40	the same ketone as above: 48

[1] For the structures of allylating agents **1**, see Figure 1. [2] The reactions with *n*-octylzinc iodide were performed under the following conditions: **1** (1 mmol), *n*-octylzinc iodide (2.5 mmol, generated *in situ* from 2.5 mmol of *n*-octyl iodide and zinc–copper couple in 5 mL of THF in the presence of 11.3 mmol of HMPA), and $Pd(PPh_3)_4$ (0.05 mmol) under 1 atm of CO (a balloon). [3] The reactions with diethylzinc were performed under the following conditions: **1** (1 mmol), diethylzinc (1.5 mmol, 1.5 M solution in either *n*-hexane or THF), and $Pd(PPh_3)_4$ (0.05 mmol) under 1 atm of CO (a balloon) in a given solvent. [4] THF, tetrahydrofuran; HMPA, hexamethylphosphoric triamide. [5] Unless otherwise specified, conversion is 100%. Yields are for the isolated, spectroscopically homogeneous products, based on the conversion of **1**. [6] The similar reaction using **1f**, in place of **1f'**, was very slow (less than 10% conversion), and no ethyl (4-isopropenyl-1-cyclohexenyl)-methyl ketone was detected.

coordination) between the heteroatoms of **2**, **5**, and **9** and metal salts (Pd^{2+} and/or Zn^{2+}) in some intermediates, but are quite general for the carbonylative coupling reaction with a range of organozinc halides.

Just one fact that the reaction of γ,γ-dimethylallyl benzoate with γ-zincio ester provides the γ-substituted product exclusively (run 7, Table 3), while those with β-zincio ester (run 5, Table 1) and octylzinc iodide (run 3, Table 5) give rise to mixtures of the corresponding α- and γ-substituted products seems to flaw the explanation based on Scheme 2, since according to this mechanism the α-/γ-substituted product ratio for the reaction with γ-zincio ester, possessing an intermediate electron-withdrawing ability, should be in between the ratios for those with β-zincio ester and octylzinc iodide.

These reactions, however, were undertaken under different reaction conditions because each organozinc reagent required the different amounts of HMPA for the optimization. Accordingly, in order to compare the product ratios on the same ground, we examined the reaction of γ-zincio ester under the same conditions (run 8, Table 3) as those applied to β-zincio ester and octylzinc iodide (2.5 equiv of organozinc reagent, 11.3 equiv of HMPA, relative to **1d**, in THF), and found that under such conditions γ-zincio ester indeed furnished the α-substituted product **7d** in just an expected amount: α/γ ratio being 11/51 for β-zincio ester, 21/48 for γ-zincio ester, and 42/40 for octylzinc iodide.

These results, together with a significant dependence of the α-/γ-substituted product ratio on the amount of HMPA as observed for runs 1 and 2 in Table 5, evidently indicate that an increase in the amount of HMPA raises the proportion of the α-substituted products relative to the γ-substituted products. However, the mechanistic role that HMPA plays in accelerating the rearrangement process (via **VI**) relative to the reductive elimination process (via **V** and/or **VI**, Scheme 2) is not clear at present.

It is frequently pointed out that dialkylzincs display completely different reactivity from alkylzinc halides.[16] In the present carbonylative coupling reaction, diethylzinc also showed quite different reactivity and product selectivity (runs 5–7, Table 5). The reaction does not necessarily require HMPA as a cosolvent and proceeds in either toluene–hexane or toluene–THF at 0 °C (runs 5, 6, Table 5). The reaction with cinnamyl benzoate provided ethyl *trans*-3-phenyl-2-propenyl ketone as a sole product in 78% yield (run 5, Table 5), and neither *cis*-3-phenyl-2-propenyl nor 1-phenyl-2-propenyl isomer was formed at all (cf., run 10, Table 3, and run 4, Table 5). The reaction with cinnamyl benzoate, when undertaken at room temperature or in the presence of HMPA, provided complex mixtures of products, containing only 20–30% of ethyl 3-phenyl-2-propenyl ketone at most. On the other hand, diethylzinc nicely reacted with diethyl perillyl phosphate (**1f'**) either in the absence (at 0 °C, run 6) or in the presence of HMPA (at room temperature, run 7, Table 5) to give the expected unsymmetrical ketone almost in the same yields.

Effects of HMPA on the Reaction Course. As mentioned shortly beforehand, the yields of unsymmetrical ketones are strongly affected by the amount of HMPA (Table 2). For example, in the presence of 11.3 equiv of HMPA, the reaction of β-zincio ester **2** and allyl benzoate (**1a**) provided ketone **3a** in 62% isolated yield together with diethyl 4-oxopimelate **14a** in 12% yield (run 4, Table 2), while in the absence of HMPA, no **3a** was produced at all (run 1, Table 2). In the latter reaction, instead, was obtained a mixture of two kinds of lactones **12a** (9%) and **13a** (59%) and diethyl 4-oxopimelate (**14a**, 21%)[17] (eq 4 in Scheme 3).

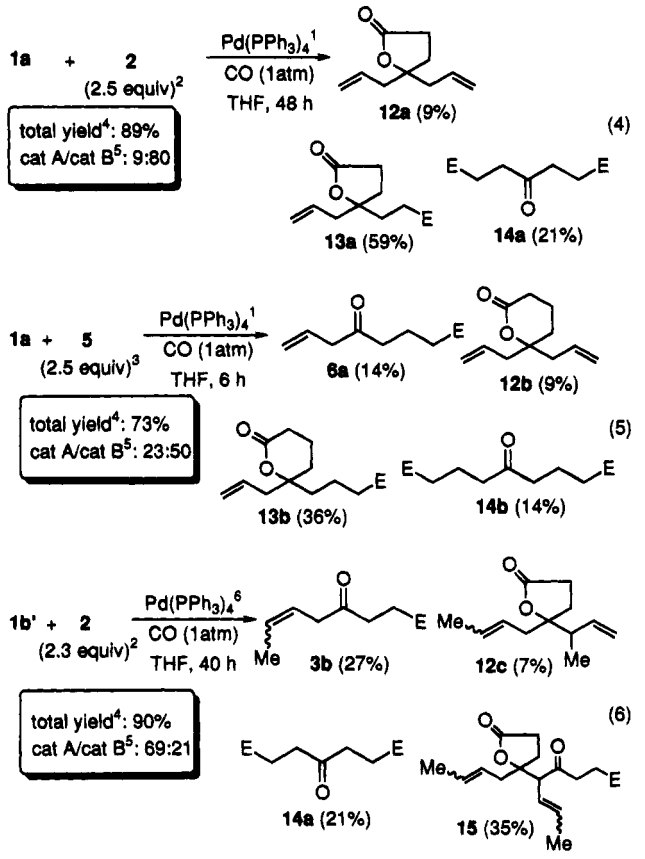
Judging from the close similarity of the structure of the major lactone **13a** to that of the unsymmetrical ketone **3a**, **13a** might be considered to be formed via the chemoselective nucleophilic attack of β-zincio ester **2** to the keto carbonyl group of **3a**, followed by the lactonization of the thus formed diethyl γ-allyl-γ-hydroxypimelate. This is not the case, however, since β-zincio ester has proven to be a very poor nucleophile and even does not react with aldehydes under such reaction conditions as in eq 4.[12c,d]

A similar but slightly more complicated result was observed for the reaction of allyl benzoate and γ-zincio ester *in the absence of HMPA* (eq 5), where, in addition to the two kinds of lactones (**12b** and **13b**) and a symmetric keto diester **14b**, the three-component coupling product **6a** was isolated (14%).

(16) (a) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49–69. (b) Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Schreiber, S. L., Eds.; Pergamon: Oxford, U.K., 1991; Vol. 1, Chapter 1.7.

(17) Aoki, S.; Nakamura, E. *Tetrahedron* **1991**, *47*, 3935–3946.

Scheme 3. Pd^0-Catalyzed Coupling Reaction of Allylic Benzoates 1, Organozincs 2 and 5, and Carbon Monoxide in the Absence of HMPA[a]

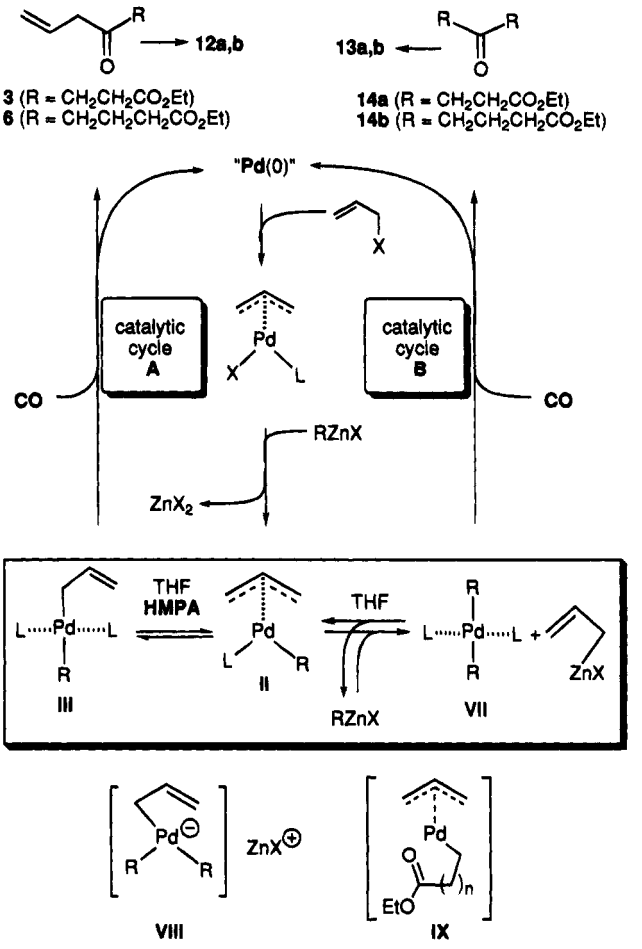


[a] (1) Unless otherwise specified, reactions were undertaken under the following conditions: allylic benzoate **1a** or **1b'** (2.5 mmol), organozinc **2** or **5** (an indicated amount, relative to **1**), and $Pd(PPh_3)_4$ (0.125 mmol, 0.05 equiv, relative to **1**) in THF (12 mL) under 1 atm of CO (a balloon) at room temperature; (2) β-zincio ester (**2**), free from HMPA, was prepared from 6.25 mmol of ethyl β-iodopropionate and zinc–copper couple in THF; (3) γ-zincio ester (**5**), free from HMPA, was prepared from 6.25 mmol of ethyl γ-iodobutyrate in THF according to the literature (Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, *56*, 1445); (4) yields were determined for the isolated, spectroscopically homogeneous products based on the reaction mechanism proposed in Scheme 3, taking **1** as a standard (see text); (5) the figures of cat. A/cat. B are meant to refer to the ratios of the combined isolated yields of the products (**3** + **6** + **12** + **15**) formed via the catalytic cycle A to those of the products (**13** + **14**) formed via the catalytic cycle B (see text and Scheme 4); (6) the reaction was carried out at room temperature for 45 h then at 35 °C for 40 h.

As mentioned previously, β-zincio ester **2** undergoes carbonylative coupling with crotyl benzoate to give unsymmetrical ketone **3b** selectively *in the presence of 11.3 equiv of HMPA* (run 3, Table 1). *In the absence of HMPA*, the same reaction provided **3b** in 27% yield (eq 6). The other products isolated were two kinds of lactones **12c** (7%) and **15** (35%) and diethyl 4-oxopimelate (**14a**, 21%). Taking into consideration that the lactone **15** as being most likely the self-aldol product of **3b** and the combined isolated yield of **3b** and **15** as amounting to 62%, the difference in the product distribution between the reactions in the absence and presence of HMPA for the combination of **1b'** and **2** is not as large as those for the combinations of **1a** and **2** and **1a** and **5**.

These contrasting results between in the presence and in the absence of HMPA (cf., run 1, Table 1, and eq 4; run 3, Table 1, and eq 6; runs 1–3, Table 3, and eq 5) might be rationalized according to the mechanism outlined in Scheme 4. In this scheme, π-allylalkylpalladium complex **II** serves as a common, pivotal intermediate through which catalytic cycles A and B diverge depending on the presence and absence of HMPA. HMPA might work as a ligand (L) and accelerate an interconversion between π-allylalkyl- (**II**) and σ-allylalkylpalladium complexes **III**, through the latter, a carbonylative coupling of allyl and alkyl groups proceeds to provide unsymmetrical ketones, e.g., **3** and **6** (catalytic cycle A, see also Scheme 2) and Pd(0) species. In the absence of HMPA, on the other hand, we assume that an alkyl–allyl exchange reaction takes place between **II** and an organozinc species, being present always in a large excess relative to **II**, and gives rise to the mixture of symmetrically substituted dialkylpalladium **VII** and allylzinc species (X = iodide or benzoate) (catalytic cycle B). The carbonylation of the intermediate **VII** may produce the symmetric keto diester **14** and regenerate the Pd(0) species. In other words, in the catalytic cycle B, overall, 1 mol of π-allylpalladium and 2 mol of organozinc react to furnish a mixture of **VII** and allylzinc species one mole each.[18]

Scheme 4. Catalytic Cycle for Pd^0-Catalyzed Multicomponent Connection Reaction



On the basis of this assumption, the results shown in eq 4 may be rationalized as follows. Diethyl 4-oxopimelate (**14a**) is formed by the carbonylation of **VII** (R = $(CH_2)_2CO_2Et$, catalytic cycle B). Most of allylzinc species, generated in an equal amount to **VII**, may react with **14a** chemoselectively at the keto carbonyl group and provide diethyl γ-allyl-γ-hydroxypimelate, which spontaneously

(18) Yasui, K.; Goto, Y.; Yajima, T.; Taniseki, Y.; Fugami, K.; Tanaka, A.; Tamaru, Y. *Tetrahedron Lett.* **1993**, *34*, 7619–7622.

undergoes lactonization to provide **13a** as the major product. The rest of the allylzinc may react with unsymmetrical ketone **3a**, generated in a small amount by the catalytic cycle A, and furnish **12a** according to the similar processes to the formation of **13a**. The results shown in eqs 5 and 6 may also be explained in a similar way.

Here it should be noted that the sums of the products derived from allylation with allylzinc (**12** + **13**) roughly correspond to the sums of the symmetric keto diesters and their allylation derivatives (**14** + **13**), which seem to support the generation of **VII** and allylzinc species in the same amounts through the proposed alkyl−allyl exchange reaction (Scheme 4).

An unsymmetrical substitution with *trans*-crotyl and α-methallyl groups at the γ-position of the lactone **12c** (eq 6) seems to further support the mechanism. Since the crotylzinc species is known to react with carbonyls selectively at the allylic carbon substituted with methyl group,[18,19] the α-methallyl substituent in **12c** may be regarded as being introduced by the reaction of crotylzinc with **3b**.

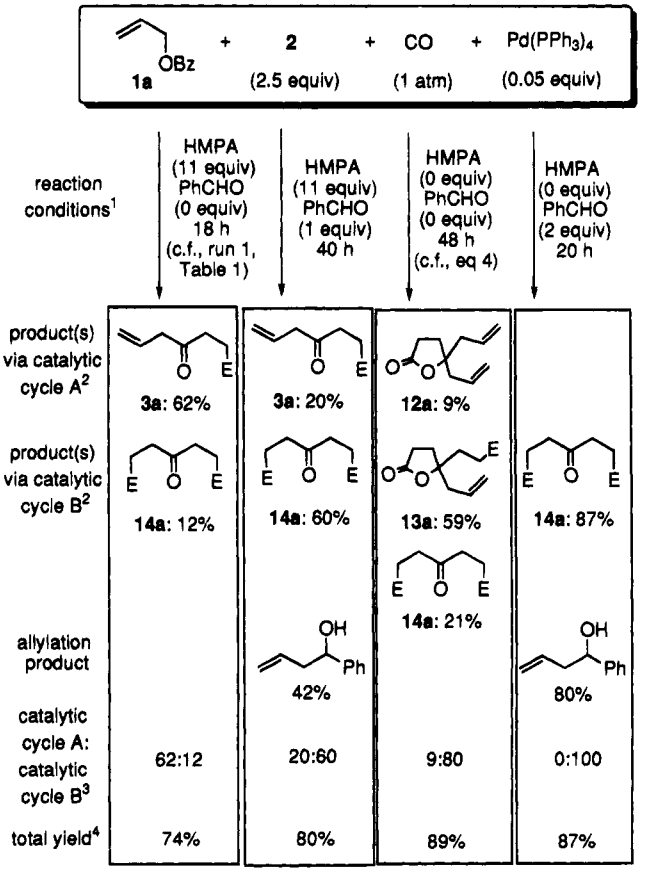
The calculation of the yields of products (**12**, **13**, and **14**) may be rather confusing, since these products are composed of zincio esters and allylating agents in varying ratios. The yields listed were calculated based on the stoichiometry expected from the mechanism shown in Scheme 4, taking allylic benzoate **1** as a standard. That is, mol of an allylic benzoate corresponds to 1 mol of an unsymmetrical ketone **3** or **6** (via the catalytic cycle A), while 1 mol of an allylic benzoate corresponds to 1 mol of a symmetric keto diester **14a** or **14b**, although no allyl groups are incorporated in this product (catalytic cycle B). The lactones **12** were regarded as the derivatives of unsymmetrical ketones **3** and **6**. The lactones **13** were counted as the derivatives of symmetrical keto diesters **14**. The combined isolated yields of products shown in eqs 4−6, despite its apparent complexity of the reaction, are remarkably high.

On the basis of the yields and types of products, we might be able to estimate the relative extent to which the catalytic cycles A and B contribute to the reactions under the specified conditions. For example, in the case of the reaction shown in eq 4, the ratio of catalytic cycles A to B is estimated to be 9:80 (the yield of **12a**:the combined yields of **13a** and **14a**). Similarly the ratios for the reaction shown in eqs 5 and 6 are determined to be 23:50 [(**6a** + **12b**):(**13b** + **14b**)] and 69:21 [(**3b** + **12c** + **15**):**14a**], respectively. These values suggest that the ratio of the catalytic cycles A to B depends only slightly on the kind of organozincs (eqs 4 vs 5) but largely on the kind of allylating agents (eqs 4 vs 6).

One might expect that the equilibrium shown in a rectangle in Scheme 4 shifts to the right by conducting reactions in the presence of an appropriate electrophile that can readily react with allylzinc species and remove it from the equilibrium mixture. Furthermore, it might be expected that under such conditions both the unsymmetrical (**3** and **6**) and symmetrical ketones **14**, produced via carbonylation through **III** and **VII**, respectively, might remain intact and could be isolated after workup. Indeed, under the similar reaction conditions to the run 1 in Table 1, *in the presence of 1 equiv of benzaldehyde*, were obtained diethyl 4-oxopimelate **14a** and 1-phenyl-3-buten-1-ol, an allylation product of benzaldehyde, in

(19) (a) Gross, B.; Prévost, C. *Bull. Soc. Chim. Fr.* **1967**, 3610−3614. (b) Miginiac-Groizeleau, L.; Miginiac, P.; Prévost, C. *Bull. Soc. Chim. Fr.* **1965**, 3560−3565.

Scheme 5. Pd⁰-Catalyzed Coupling Reaction of β-Zincio ester (2), Allyl Benzoate (1a), and Carbon Monoxide in the Presence or Absence of HMPA and Benzaldehyde[a]



[a] (1) All reactions were undertaken at room temperature in THF; (2) E stands for ethoxycarbonyl group; (3) the ratio is meant to refer to the ratio of the combined isolated yields of the products (**3a** + **12a**) formed via the catalytic cycle A to those of the products (**13a** + **14a**) formed via the catalytic cycle B, shown in Scheme 3; (4) the total yield (**3a** + **12a** + **13a** + **14a**) is calculated according to the mechanism outlined in Scheme 3, taking **1a** as a standard (see text).

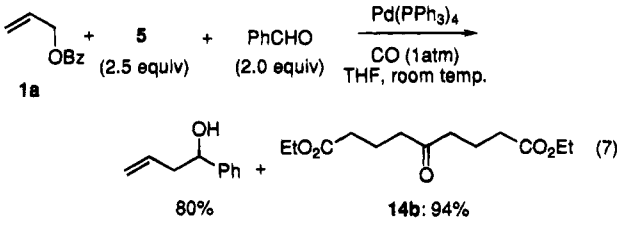
60% and 42% yields, respectively, together with unsymmetrical ketone **3a** (20%) (the second column in Scheme 5).

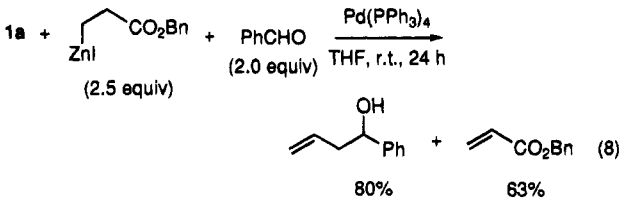
For the ease of comparison, the results discussed already were arranged in the first and third columns in Scheme 5 (run 1, Table 1, and eq 4, respectively). Comparison of the first and second columns clearly reveals that in the absence and presence of 1 equiv of benzaldehyde, the ratio of catalytic cycles A to B has changed from 62:12 (**3a**:**14a**) to 20:60 (**3a**:**14a**).

Furthermore, *in the absence of HMPA and in the presence of 2 equiv of benzaldehyde*, only the two products, **14a** and homoallyl alcohol, both being derived from the catalytic cycle B, were obtained in quantitative yields (the fourth column, Scheme 5). The apparent gradual change in the ratios of catalytic cycles A to B, depending the amounts of HMPA and benzaldehyde (Scheme 5), is consistent with the mechanism proposed in Scheme 4 and seems to support further an intervention of the equilibrium shown in a rectangle.

The similar dependence of the ratio of catalytic cycles A to B on the amounts of HMPA and benzaldehyde was observed for the reactions of γ-zincio ester and allyl benzoate: 68:0 (2.5 equiv of HMPA, 0 equiv of benzaldehyde, run 1, Table 3), 23:50 (0 equiv of HMPA, 0 equiv

of benzaldehyde, eq 5), and 0:94 (0 equiv of HMPA, 2 equiv of benzaldehyde, eq 7). The reaction shown in eq 7 was undertaken with 2.5 equiv of γ-zincio ester and allyl benzoate *in the absence of HMPA and in the presence of 2 equiv of benzaldehyde* under the usual reaction conditions (1 atm of carbon monoxide at room temperature for 24 h). Here again symmetrical keto diester **14b** and homoallyl alcohol, due to catalytic cycle B, were obtained in quantitative yields. No products due to catalytic cycle A were detected at all.





The catalytic cycle B seems to operate even in the absence of carbon monoxide (eq 8), where an allylzinc species serves as a nucleophile as usual and reacts with benzaldehyde to provide homoallyl alcohol in good yield, while a symmetrical dialkylpalladium intermediate **VII** (R = $CH_2CH_2CO_2CH_2Ph$) provides an acrylate in 63% yield, presumably as a consequence of dehydropalladium.

As the most probable and alternative intermediate to an allylzinc species, an allyldialkylpalladate species **VIII** should be noted (Scheme 4). However, we believe that **VIII** might possibly be formed just as an intermediate during the transmetalation forming a mixture **VII** and an allylzinc species by the reaction between **II** and an alkylzinc species, and might not serve as an active allylating species, since it has been demonstrated by our other studies that the allylation of aldehydes under the conditions of catalytic cycle B displays very high regio- and stereoselectivities that might only be reconciled with a tight six-membered transition state, involving allylzinc as the four-atom constituent and aldehyde carbonyl as the two-atom constituent, where the aldehyde oxygen tightly coordinates Zn^{2+}.[18,20] The palladate **VIII** is coordinatively saturated and charged negatively and might not be able to form such a tight cyclic transition state for the reaction with aldehyde.

The high chemoselectivity of the above-mentioned allylation reaction should be noted here, showing the following reactivity order (approximate relative reactivity): aldehyde (7000) > ketone (100) ≫ ester (1).[18] The low reactivity of ester groups seems to make the catalytic cycle B viable; otherwise, the reaction might be seriously damaged by the allylation of the starting substrates, allylic benzoates **1**.

The eventful reactivity of the present carbonylative coupling reaction seems to owe its origin to the remarkable reluctance of π-allylalkylpalladium intermediate **II** toward a reductive elimination. This makes marked contrast to the fact that a variety of organolithiums, -magnesiums,[21] and even some types of organozincs [α-zincio esters (Reformatsky reagent),[22] phenylzinc halides,[23] and perfluorozinc halides][24] readily undergo a reductive elimination through species like **II**. In fact, this process has proven to be one of the basic and most useful processes in π-allylpalladium chemistry. The organozinc reagents treated in this paper, on the other hand, are indifferent to the allylation even under some typical allylation reaction conditions. For example, as reported previously,[12f] the reaction of γ-zincio ester **5** with cinnamyl benzoate in the presence of 5 mol % of tetrakis(triphenylphosphine)palladium did not provide the expected allylation product, ethyl 7-phenyl-6-heptenoate, at all; instead, it furnished the homocoupling products of these reactants, 1,4- (76%) and 1,6-diphenyl-1,5-hexadienes (6%) and diethyl suberate (38%).[12f] 1,5-Hexadienes might be rationalized to be formed via an allylation of cinnamylpalladium intermediate with cinnamylzinc[25] and diethyl suberate via a reductive elimination through **VII** (R = $CH_2CH_2CH_2CO_2Et$) (catalytic cycle B, Scheme 4).

The unusual reactivity of the π-allylalkylpalladium species **II** may become apparent further in view of the fact that vinylalkylpalladiums, phenylalkylpalladiums, and acylalkylpalladiums undergo a smooth reductive elimination, as observed for the palladium-catalyzed coupling reactions of vinyl iodides,[12g,26] aryl halides,[12g,27] and acid halides[12i,28] with organozincs, respectively.

In the cases of β- and γ-zincio esters, the kinetic stability of **II** toward a reductive elimination as well as dehydropalladation might be attributed to the chelation stabilization of the ester carbonyl oxygen to palladium^{2+} to form **IX** (n = 1 for β- and n = 2 for γ-zincio esters, Scheme 4). However, the kinetic stability of the complexes **II** is not confined to the derivatives of β- and γ-zincio esters but seems to be quite general to the other organozincs (e.g., zincio nitriles **9a–e**, octylzinc iodide) that are not capable of forming such a chelation structure.

Determination of the Stereochemical Course of the Three-Component Connection Reaction. In an effort to determine the stereochemical course of the carbonylative coupling reaction at the allylic partners, the reactions with diethyl *cis*- and *trans*-carvyl phosphates (*cis*- and *trans*-**1h**) were examined (Scheme 7). *cis*- and *trans*-Carvyl alcohols with high stereochemical homogeneity were prepared as follows (Scheme 6): Reduction of commercially obtained (±)-carvone with $LiAlH_4$–$AlCl_3$ provided a mixture of carvyl alcohols (*cis*:*trans* = 86:14) in 95% yield (process a). Iodoetherification[29]

(20) Tamaru, Y.; Tanaka, A.; Yasui, K.; Goto, S.; Tanaka, S. *Angew. Chem.*, in press.

(21) (a) Tsuji, J. *Pure Appl. Chem.* **1982**, *54*, 197–206. (b) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385–393.

(22) Boldrini, G. P.; Mengoli, M.; Tagliavini, E. *Tetrahedron Lett.* **1986**, *27*, 4223–4226.

(23) (a) Fiaud, J.-C.; Legros, J.-Y. *J. Org. Chem.* **1987**, *52*, 1907–1911. (b) Hayashi, T.; Yamamoto, A.; Hagihara, T. *J. Org. Chem.* **1986**, *51*, 723–727. (c) Chatterjee, S.; Negishi, E. *J. Org. Chem.* **1985**, *50*, 3406–3408.

(24) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186–5191.

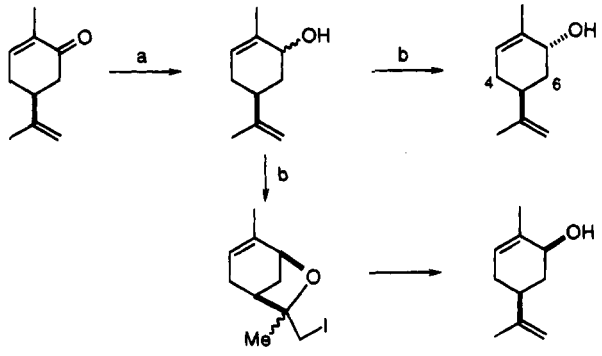
(25) Sasaoka, S.; Yamamoto, T.; Kinoshita, H.; Inomata, K.; Kotake, H. *Chem. Lett.* **1985**, 315–318.

(26) Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* **1980**, *102*, 3298–3299.

(27) Negishi, E.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821–1823.

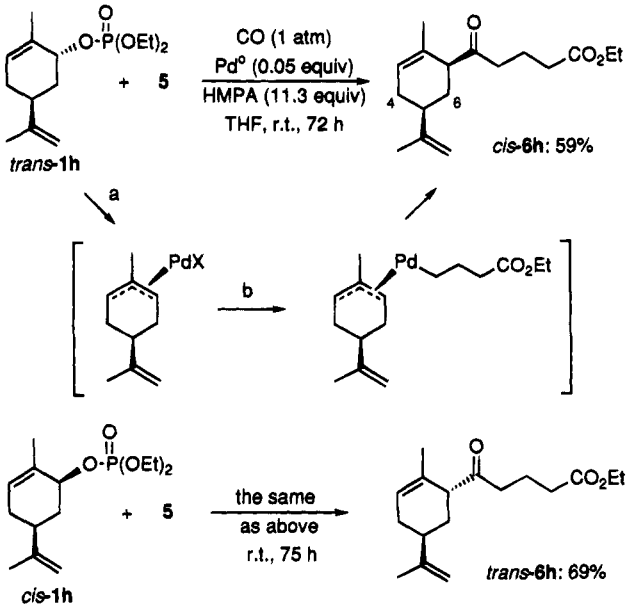
(28) (a) Negishi, E.; Bagheri, V.; Chatterjee, S.; Luo, F.-T.; Miller, J. A.; Stoll, A. T. *Tetrahedron Lett.* **1983**, *24*, 5181–5184. (b) Sato, T.; Ito, T.; Fujisawa, T. *Chem. Lett.* **1982**, 1559–1560.

Scheme 6. Preparation of Stereochemically Homogeneous *cis*- and *trans*-Carveols[a]



[a] Key: (a) $LiAlH_4$–$AlCl_3$/ether/−20 °C, 40 min, 95%, *cis*:*trans* = 86:14; (b) I_2 (2 equiv), $NaHCO_3$ (2 equiv)/ether–H_2O/0 °C, 15 h, 100%; (c) Zn(Cu) (1.5 equiv)/THF–HMPA (1.5 equiv)/reflux, 3 h, 81%, *cis*:*trans* = 98:2.

Scheme 7. Stereospecific Carbonylation with Overall Inversion of Configuration



of the alcohol mixture provided a bicyclic iodo ether, 6-(iodomethyl)-2,6-dimethyl-7-oxabicyclo[3.2.1]oct-2-ene, in a quantitative yield, keeping the *trans*-alcohol intact (process b). Reduction of the bicyclic iodo ether with zinc–copper couple yielded *cis*-carvyl alcohol, contaminated with 2% of the *trans* isomer, in 81% isolated yield (process c). The reason for the contamination with the *trans* isomer during the process c is not clear at present. Repeated experiments, using the bicyclic iodo ether rigorously purified by column chromatography and distillation, always accompany the formation of the *trans* isomer in 2–3% yields.

In order to obtain *trans*-carvyl alcohol in substantial quantity, the mixture of alcohols obtained by the process a; Scheme 6 was subjected to Mitsunobu inversion and hydrolysis. Through these transformations, carvyl alcohols enriched with *trans* isomer (*cis*:*trans* = 3:7) was obtained in 85% overall yield. Sterically homogeneous *trans*-carvyl alcohol was obtained as the remainder of the iodoetherification (process b, Scheme 6).

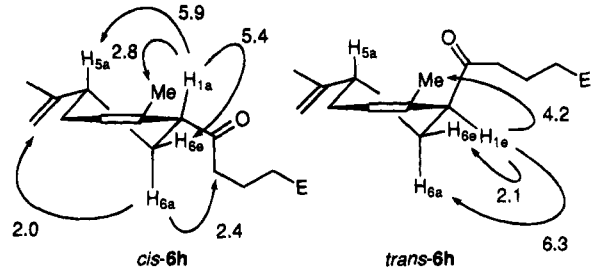


Figure 2. Nuclear Overhauser effects (%) for *cis*-**6h** and *trans*-**6h**.

The isomers of carvyl alcohols can be readily distinguished on the basis of their high-field ^1H NMR spectra (400 MHz). The resonances corresponding to H_6-axial protons in these alcohols appear at the highest fields and show characteristic coupling patterns, dt, J = 4.0 and 13.2 Hz (δ 1.61 ppm) for *trans*-carvyl alcohol and dt, J = 9.5 and 12.1 Hz (δ 1.51 ppm) for *cis*-carvyl alcohol.

cis- and *trans*-Carvyl diethyl phosphates (*cis*- and *trans*-**1h**), prepared by the reactions with 1.0 equiv of diethyl chlorophosphate and 4.0 equiv of pyridine in dichloromethane at 0 °C, were apt to undergo hydrolysis during purification by column chromatography over silica gel and were used for the coupling reactions without any purifications after usual extractive workup (Scheme 7).[30] The carbonylative coupling reaction of *trans*-carvyl phosphate (*trans*-**1h**) with γ-zincio ester (2.5 equiv) proceeded nicely by the catalysis of 5 mol % of tetrakis(triphenylphosphine)palladium in THF containing 11.3 equiv of HMPA at room temperature under 1 atm of carbon monoxide and yielded unsymmetrical ketone *cis*-**6h** as a single diastereomer in 59% overall yield from the alcohol. Under the similar conditions, *cis*-carvyl phosphate (*cis*-**1h**, contaminated with 2% of *trans*-**1h**) provided the unsymmetrical ketone *trans*-**6h**, contaminated with 2–3% of *cis*–**6h**, in 69% isolated overall yield from the alcohol.

These stereochemical outcomes clearly indicate that carbonylative coupling reaction proceeds *stereospecifically with overall inversion at the allylic stereocenters* and suggest that a sequence of steps outlined in Scheme 7 proceeds without losing stereochemical integrity. Oxidative addition to Pd(0) is known to proceed with inversion at allylic centers (process a, Scheme 7) and CO insertion to palladium–carbon bonds with retention of configuration at carbons (process c).[3c] Accordingly, the stereospecificity observed for the formation of unsymmetrical ketones **6h** requires that the transmetalation of γ-(ethoxycarbonyl)propyl group onto palladium proceeds without deteriorating the stereochemical integrity of allylpalladium intermediate (process b, Scheme 7).

The stereochemistry of *cis*- and *trans*-**6h** was determined unequivocally on the basis of 2D ^1H NMR and NOE experiments (Figure 2).[31] As anticipated from the structure, the H_{6a} proton in *cis*-**6h** appears as a quartet (ddd) with large coupling constants (J = 12.1 Hz) at 1.49 ppm. Furthermore, significant increments in the area intensities are observed for H_{5a} by irradiation at H_{1a} and for both the C_1-methylene protons of γ-(ethoxylcarbonyl)-propyl substituent and the olefinic protons of isopropenyl group by irradiation at H_{6a}. For *trans*-**6h**, no diagnostic NOE are observed by the irradiations at H_{1e} and H_{6a};

(29) (a) Tamaru, Y.; Harayama, H.; Bando, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1601–1602. (b) Tamaru, Y.; Hojo, M.; Kawamura, S.; Sawada, S.; Yoshida, Z. *J. Org. Chem.* **1987**, *52*, 4062–4072.

(30) Murahashi, S.; Taniguchi, Y.; Imada, Y.; Tanigawa, Y. *J. Org. Chem.* **1989**, *54*, 3292–3303.

(31) Breitmaier, E. *Structure Elucidation by NMR in Organic Chemistry*; Wiley: New York, 1993.

however, the coupling pattern of H_{6a}, appearing as a ddd, J = 6.6, 11.7, and 13.2 Hz, clearly supports the structure.

Conclusion

β-Zincio ester **2** (optimized with 11.3 equiv of HMPA), γ-zincio ester **5** (with 2.3 equiv or the larger amounts of HMPA), zincio nitriles **9a–e** (with 11.3 equiv of HMPA), octylzinc iodide (with 11.3 equiv or the smaller amounts of HMPA), and diethylzinc (the optimized amount of HMPA being dependent on the kind of allylating agents) undergo the palladium-catalyzed carbonylative coupling reaction with allylic benzoates or phosphates to provide unsymmetrical ketones, e.g., **3**, **6**, and **10**, in good to moderate yields (catalytic cycle A, Scheme 4).

The reactions with unsymmetrical allylating agents provide selectively those ketones with the least number of substituents at the carbons α to the carbonyl group. In some cases, especially the reactions of octylzinc iodide and ε- and ζ-zincio nitriles, all the possible regio- and stereoisomeric ketones are obtained, i.e., α-substituted allyl ketones and *cis*- and *trans*-γ-substituted allyl ketones. The proportion of the α-substituted products increases with an increase in the amounts of HMPA and also with an increase in the electron-donating ability of the organic moieties of organozinc species. The carbonylative coupling reaction with carvyl phosphates (**1h**) is stereospecific and proceeds with inversion of configurations: *trans*- and *cis*-**6h** are obtained exclusively from *cis*- and *trans*-**1h**, respectively.

In the absence of HMPA, the reaction feature changes dramatically and the catalytic cycle B predominates over the catalytic cycle A (Scheme 4). In the catalytic cycle B, symmetrical keto diesters **14** are formed as primary products, which react further with allylzinc species, generated through this catalytic cycle, to give lactones **13**. The catalytic cycle B is favored especially in the presence of carbonyl compounds. As an extreme, in the presence of benzaldehyde and in the absence of HMPA, the catalytic cycle B becomes as an exclusive pathway and both the symmetric keto diesters **14** and the allylation product of benzaldehyde are produced in quantitative yields.

Experimental Section

Melting points were determined with Yanagimoto micro melting point apparatus and were not corrected. Unless otherwise specified, short-path (bulb-to-bulb) distillations were carried out in a kugelrohr apparatus. In these cases, boiling points are meant to refer to the oven temperature. Microanalysis were performed by the Microanalysis Center of Nagasaki University. Analyses agreed with the calculated values within ±0.3%. High-resolution mass spectra (HRMS) were measured with JEOL JMS-DX303. Infrared spectra were measured with a JASCO A-100 infrared spectrophotometer. Proton magnetic resonance spectra were determined either at 60 MHz on a JEOL JNM-PMX60 or at 400 MHz on a JEOL-GX400 instrument with tetramethylsilane as an internal standard. ^{13}C NMR spectra were determined at 100 MHz on a JEOL-GX400 instrument with tetramethylsilane as an internal standard. Chemical shift values were given in ppm downfield from an internal standard. R_f values were determined over Merck Kiesel gel $60F_{254}$.

Solvents and Reagents. Tetrahydrofuran and diethyl ether were dried and distilled from benzophenone and sodium immediately prior to use under a nitrogen atmosphere. Hexamethylphosphoric triamide (HMPA), dimethylformamide (DMF), and dimethylacetamide (DMA) were distilled over calcium hydride under reduced pressure. Toluene was distilled over Na. Benzene, dichloromethane, pyridine, and triethylamine were distilled over calcium hydride. Chlorotrimethylsilane was distilled from Na and kept over pieces of Na under N_2. Benzaldehyde was distilled under reduced pressure prior to use. Diethylzinc (2 M *n*-hexane solution from Wako Chemical Co.; neat from Aldrich), zinc powder (reagent grade), $LiAlH_4$, $CuSO_4$, $AlCl_3$, benzoyl chloride, *p*-(methoxycarbonyl)benzoyl chloride, octyl bromide, diethyl chlorophosphate, (*R*)-(−)-carvone, (*S*)-(−)-perillyl alcohol, 3-chloropropanenitrile, 4-chlorobutanenitrile, 5-chloropentanenitrile, and 7-bromoheptanenitrile were purchased and used without further purification.

Preparation of Ethyl ω-Iodoalkanoates. Ethyl β-iodopropionate and γ-iodobutyrate were prepared according to the literature.[32]

General Procedure for the Preparation of ω-Iodoalkanenitriles. 3-Iodopropanenitrile, 4-iodobutanenitrile, 5-iodopentanenitrile, and 7-iodoheptanenitrile were prepared as follows: An appropriate ω-haloalkanenitrile (0.1 mol), obtained commercially, and NaI (45 g, 0.3 mol) was stirred and refluxed in acetone (100 mL) for 2 days under N_2. After distilling off the solvent, the residue was diluted with water and extracted with ethyl acetate (200 mL + 100 mL). The organic extracts were successively washed with 1 M $Na_2S_2O_3$ and saturated $NaHCO_3$, dried ($MgSO_4$), concentrated, and distilled under reduced pressure to give an iodonitrile as a colorless liquid. The yields were almost quantitative (80–95%). 6-Iodohexanenitrile was prepared in a similar way using 6-bromohexanenitrile, prepared as follows: A suspension of KCN (6.68 g, 0.1 mol) in H_2O–ethanol (10–35 mL) was refluxed with 1,5-dibromopentane (23 g, 0.1 mol) for 3 h. After dilution with water (45 mL), the mixture was extracted with chloroform (3 × 50 mL). The combined extracts were successively washed with saturated $CaCl_2$–water (50 mL, 1:1 v/v) and water (50 mL) and dried ($MgSO_4$). The solvents were distilled off under atmospheric pressure, and the residue was distilled twice under reduced pressure (77–79.5 °C/0.6 mmHg) to give 6-bromohexanenitrile as a colorless liquid in 33% yield.

Preparation of *cis*- and *trans*-Carveol (Scheme 6): Reduction of (*R*)-(−)-Carvone with $LiAlH_4/AlCl_3$. Into a round-bottomed flask, purged with N_2, were placed $AlCl_3$ (1.33 g, 10 mmol) and $LiAlH_4$ (1.14 g, 30 mmol). With cooling in an ice bath, cold, dry ether (100 mL) was added by cannulation technique, and the mixture was stirred at 0 °C until the color of the suspension turns from gray to white. After the mixture was allowed to cool to −20 °C, (*R*)-(−)-carvone (9.01 g, 60 mmol) dissolved in dry THF (60 mL) was added slowly over 40 min period and the mixture was stirred at the same temperature for additional 2 h. The mixture was transferred into an Erlenmeyer flask and diluted with dichloromethane (140 mL). At −20 °C, NaF (16.8 g, 0.4 mol) and water (8.7 mL) were successively added with well swirling. The resultant mixture was filtered with suction through a Celite pad over a glass filter, and the filtrate was concentrated *in vacuo*. Kugelrohr distillation (60 °C/0.1 mmHg) provided carveol (8.63 g, 95% yield) as a mixture of *cis*:*trans* = 86:14. **Enrichment in *trans*-Carveol.** Into a stirred solution of carveol (3.05 g, 20.1 mmol, *cis*:*trans* = 86:14), triphenylphosphine (10.5 g, 40 mmol), and formic acid (1.51 mL, 40 mmol) in dry THF (50 mL) was added a solution of diethyl azodicarboxylate (6.97 g, 40 mmol) in THF (60 mL) at room temperature over 30 min period. After stirring under N_2 for 4 h at room temperature, the solvent was removed *in vacuo*, and the sticky solid residue was triturated with hexane–ethyl acetate (4:1, v/v, 2 × 100 mL). The combined washings were filtered and concentrated, and the residue was purified roughly by means of short path column chromatography over silica gel (hexane:ethyl acetate = 4:1, v/v) to give a mixture of *cis*- and *trans*-carvyl formates (R_f = 0.86, hexane:ethyl acetate = 4:1, v/v). The mixture of formates was dissolved in MeOH (100 mL) containing NaOH (0.95 g, 24 mmol), and the resultant mixture was stirred at room temperature for 5 min. The solvent was removed *in vacuo*, and the residue was dissolved in ether (140 mL). The ethereal solution was washed successively with 2 N NaOH, saturated $NaHCO_3$, and brine and dried ($MgSO_4$). Purification

(32) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Org. Synth.* **1988**, *67*, 98–104.

by column chromatography over silica gel (R_f = 0.49, hexane:ethyl acetate = 4:1, v/v), followed by kugelrohr distillation (95 °C/0.55 mmHg), provided a mixture of *cis*- and *trans*-carveol in a ratio of 30:70 in 85% overall yield.

***trans*-Carveol.** Into a heterogeneous mixture of ether (50 mL)–H_2O (20 mL) containing *trans*-enriched carveol (2.48 g, 16.3 mmol, *cis*:*trans* = 30:70) and $NaHCO_3$ (2.74 g, 32.6 mmol), cooled in an ice bath, was added I_2 (8.27 g, 32.6 mmol) in one portion.[28] After allowing to stir at 0 °C for 15 h, the mixture was diluted with ethyl acetate (100 mL) and the resultant solution was successively washed with aqueous $Na_2S_2O_3$, saturated $NaHCO_3$, and brine. Drying over $MgSO_4$, evaporation of the solvents, and purification by column chromatography over silica gel, followed by distillation of the collected column fractions under reduced pressure with a kugelrohr apparatus provided pure *trans*-carveol (R_f = 0.49, hexane:ethyl acetate = 4:1, v/v; bp 78 °C/0.2 mmHg, 41% yield based on the content of the *trans* isomer of the starting carveols) and 6-(iodomethyl)-2,6-dimethyl-7-oxabicyclo[3.2.1]oct-2-ene (R_f = 0.62, hexane:ethyl acetate = 4:1, v/v; bp 90 °C/0.1 mmHg, 100% based on the content of the *cis* isomer of the starting carveols). ***trans*-Carveol**: bp 78 °C/0.2 mmHg: IR (neat film) 3324 (m), 3080 (w), 2916 (s), 1651 (m), 1440 (m), 1167 (w), 1053 (s), 1032 (m), 960 (m), 941 (m), 884 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.59 (br s, 1 H), 1.61 (dt, J = 4.0, 13.2 Hz, 1 H), 1.75 (s, 3 H), 1.81 (br s, 3 H), 1.88 (m, 1 H), 1.94 (br d, J = 13.2 Hz, 1 H), 2.15 (m, 1 H), 2.33 (m, 1 H), 4.03 (br s, 1 H), 4.73 (br, s, 1 H), 4.75 (br s, 1 H), 5.59 (br d, J = 5.5 Hz, 1 H). **6-(Iodomethyl)-2,6-dimethyl-7-oxabicyclo[3.2.1]oct-2-ene:** bp 90 °C/0.1 mmHg; IR (neat film) 2960 (s), 2934 (s), 1448 (s), 1169 (m), 1142 (w), 1087 (m), 1028 (s), 995 (s), 958 (s), 940 (m), 910 (m), 901 (m) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.41 (s, 3 H), 1.61–1.80 (br s, 3 H), 1.81–2.60 (m, 5 H), 3.22 (s, 2 H), 4.02 (m, 1 H), 5.20 (m, 1 H).

***cis*-Carveol.** A flask containing zinc–copper couple (929 mg, 14.1 mmol)[33] and a stirring bar was purged with N_2. Into this were added dry THF (10 mL), HMPA (2.45 mL, 14.1 mmol), and 6-(iodomethyl)-2,6-dimethyl-7-oxabicyclo[3.2.1]-2-ene (2.62 g, 9.4 mmol) via syringes, and the mixture was stirred vigorously for 1.5 h under reflux. After being allowed to cool to room temperature, the mixture was diluted with ethyl acetate (100 mL) and washed successively with 2 N HCl, saturated $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$) and concentrated, and the residue was subjected a short path column chromatography over silica gel (hexane:ethyl acetate = 6:1, v/v). The collected fractions were concentrated *in vacuo* and distilled by a kugelrohr apparatus (95 °C/0.4 mmHg) to provide *cis*-carveol contaminated with 2–3% of the *trans* isomer in 81% yield: bp 95 °C/0.4 mmHg; IR (neat film) 3340 (m), 3076 (w), 2916 (m), 1650 (m), 1454 (m), 1200 (m), 1040 (m), 986 (s), 916 (m), 887 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.51 (dt, J = 9.5, 12.1 Hz, 1 H), 1.70 (br s, 1 H), 1.74 (s, 3 H), 1.76 (br s, 3 H), 1.95 (m, 1 H), 2.07 (m, 1 H), 2.16 (ddm, J = 12.1, 5.9 Hz, 1 H), 2.27 (m, 1 H), 4.19 (m, 1 H), 4.73 (br s, 2 H), 5.50 (m, 1 H).

General Procedure for the Preparation of Allylic Benzoates. Allyl (**1a**), α-methylallyl (**1b**), crotyl (**1b'**), β-methylallyl (**1c**), γ,γ-dimethylallyl (**1d'**), cinnamyl (**1e**), perillyl (**1f**), and 2-cyclohexenyl benzoates (**1g**) were prepared in quantitative yields according the following procedure: Into a solution of benzoyl chloride (7.73 g, 55 mmol) in ether (50 mL) were added successively an appropriate allylic alcohol (50 mmol) and triethylamine (55 mmol) at 0 °C under N_2. After stirring at 0 °C for 2 h and then at room temperature overnight, the mixture was diluted with ethyl acetate (70 mL) and washed successively with 2 HCl (2 × 10 mL), saturated $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$) and concentrated, and the residue was distilled under reduced pressure with a kugelrohr apparatus. 2-Cyclohexenyl *p*-(methoxycarbonyl)benzoate (**1g'**) was prepared similarly using *p*-(methoxycarbonyl)benzoyl chloride in place of benzoyl chloride, and purified by recrystallization (mp 76.0–77.0 °C from methanol). α,α-Dimethylallyl benzoate (**1d**) was prepared as follows: Into a suspension of NaH (60 mmol), washed with dry ether, in DMF (50 mL) was added α,α-dimethylallyl alcohol (4.31 g, 50 mmol) at 0 °C under N_2. The mixture was stirred at 0 °C for 10 min and then at room temperature for 15 min. After the mixture was allowed to cool to 0 °C, benzoyl chloride (8.42 g, 60 mmol) was added and the resultant mixture was stirred at the same temperature for 2 h then at room temperature overnight. After dilution with hexane (150 mL), the mixture was successively washed with cold, dilute aqueous ammonia (5 × 20 mL). Drying over $MgSO_4$, removal of the solvents, and distillation under reduced pressure (82 °C/0.01 mmHg) provided **1d** as a colorless oil in 84% yield.

General Procedure for the Preparation of Allylic Diethyl Phosphates. Into a solution of an appropriate allylic alcohol (40 mmol) and pyridine (7.9 mL, 0.2 mol) in dichloromethane (40 mL) was added diethyl chlorophosphate (7.3 g, 42 mmol) at 0 °C under nitrogen. The resulting white slurry was stirred at 0 °C for 1 h and then at room temperature for 30 min. The mixture was diluted with ether (100 mL), washed successively with 2 N HCl (3 × 20 mL), brine (20 mL), and saturated $NaHCO_3$ (2 × 20 mL), and dried over $MgSO_4$. The solvents were removed *in vacuo* to give an allylic diethyl phosphate as a colorless liquid. Diethyl perillyl phosphate (**1f'**, R_f = 0.1, hexane:ethyl acetate = 4:1, v/v) was purified by column chromatography over silica gel. 2-Cyclohexenyl (**1g''**) and carvyl diethyl phosphates (*cis*- and *trans*-**1h**) decomposed during purification by column chromatography over silica gel and were used without purification. In all cases, the (crude) yields were almost quantitative (90–100%).

Diethyl perillyl phosphate (1f'): IR (neat film) 2979 (s), 2927 (s), 1676 (w), 1650 (m), 1371 (m), 1275 (s), 1100 (m), 1030 (s), 983 (s), 884 (m) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.33 (t, J = 7.0 Hz, 6 H), 1.55–2.37 (m, 10 H), 3.97 (q, J = 7.0 Hz, 2 H), 4.10 (q, J = 7.0 Hz, 2 H), 4.41 (br s, 1 H), 4.54 (br s, 1 H), 4.70 (br s, 2 H), 5.79 (m, 1 H).

2-Cyclohexenyl diethyl phosphate (1g''): IR (neat film) 3024 (w), 2978 (m), 2930 (m), 1390 (m), 1260 (s), 1166 (m), 1032 (s), 985 (s), 891 (m) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.15–2.21 (m, 6 H), 1.32 (t, J = 7.1 Hz, 6 H), 3.95 (q, J = 7.1 Hz, 2 H), 4.09 (q, J = 7.1 Hz, 2 H), 4.76 (m, 1 H), 5.55–6.05 (m, 2 H).

***cis*-Carvyl diethyl phosphate (*cis*-1h)**: IR (neat film) 3079 (w), 2978 (s), 2912 (s), 1650 (m), 1390 (m), 1260 (s), 1167 (m), 1078 (s), 1028 (s), 995 (s), 908 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.34 (t, J = 7.1 Hz, 6 H), 1.67 (m, 1 H), 1.72 (s, 3 H), 1.76 (br s, 3 H), 1.96 (m, 1 H), 2.07 (m, 1 H), 2.22–2.38 (m, 2 H), 4.12 (quint, J = 7.1 Hz, 2 H), 4.14 (quint, J = 7.1 Hz, 2 H), 4.73 (br s, 1 H), 4.74 (br s, 1 H), 4.96 (m, 1 H), 5.58 (m, 1 H).

***trans*-Carvyl diethyl phosphate (*trans*-1h)**: IR (neat film) 3072 (w), 2974 (m), 2916 (m), 1650 (m), 1390 (m), 1370 (m), 1260 (s), 1096 (m), 1030 (s), 977 (s), 902 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.34 (t, J = 7.1 Hz, 3 H), 1.35 (t, J = 7.1 Hz, 3 H), 1.64 (ddd, J = 14.3, 12.8, 3.7 Hz, 1 H), 1.74 (s, 3 H), 1.81 (br s, 3 H), 1.91 (m, 1 H), 2.12–2.24 (m, 2 H), 2.41 (m, 1 H), 4.11 (quint, J = 7.1 Hz, 2 H), 4.13 (quint, J = 7.1 Hz, 2 H), 4.71–4.78 (m, 3 H), 5.71 (m, 1 H).

Typical Examples of Procedures for the Carbonylative Coupling Reactions. Case 1 (run 1, Table 1). A typical procedure for the reactions of β-zincio ester **2** and allylic benzoates **1** in the presence of HMPA: A mixture of ethyl β-iodopropionate (570 mg, 2.5 mmol), zinc–copper couple (247 mg, 3.75 mmol),[33] and HMPA (1.97 mL, 11.3 mmol) in THF (5 mL) was refluxed for 3 h under N_2 with well stirring.[32] After being allowed to cool, the mixture was transferred by cannulation technique into a flask containing a solution of allyl benzoate (**1a**, 162 mg, 1 mmol) and tetrakis(triphenylphosphine)palladium (57.8 mg, 0.05 mmol) in THF (5 mL) under an atmosphere of carbon monoxide (a balloon). The mixture was stirred at room tempearture for 18 h and then poured into ethyl acetate (70 mL). The mixture was washed successively with 2 N HCl (2 × 10 mL), saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by column chromatography over silica gel (benzene as a eluent) to give ethyl 4-oxo-6-heptenoate (**3a**, R_f = 0.44, benzene:ethyl acetate = 32:1, v/v) and diethyl 4-oxopimelate (**14a**, R_f = 0.08) in 62 and 12% yields, respectively.

(33) Smith, R. D.; Simmons, H. E. *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. 5, pp 855–858.

Case 2 (Table 2). A typical procedure for the reactions of β-zincio ester **2** and allyl benzoate (**1a**) in the presence of varying amounts of HMPA: A mixture of ethyl β-iodopropionate (570 mg, 2.5 mmol) and zinc–copper couple (247 mg, 3.75 mmol) in THF (5 mL) was refluxed for 5 h with stirring N_2. After the mixture was allowed to cool to room temperature, the indicated amount of HMPA, relative to allyl benzoate (**1a**), was added. This mixture was subjected to carbonylative coupling reaction following the similar procedure indicated in case 1. The reaction was monitored by TLC (Merck Kiesel gel $60F_{254}$), following the relative intensity of **1a** to those of the product(s) as an indication of the progress of the reaction. The conversion was determined on the basis of the recovered **1a** by column chromatography over silica gel.

Case 3 (run 3, Table 3). A typical procedure for the reactions of γ-zincio ester **5** and allylic benzoates **1** in the presence of HMPA and chlorotrimethylsilane: A mixture of ethyl γ-iodobutyrate (726 mg, 3.0 mmol), zinc–copper couple (297 mg, 4.5 mmol), and HMPA (782 μL, 4.5 mmol) in THF (5 mL) was refluxed for 3 h with stirring under N_2. After being allowed to cool, the mixture was transferred by cannulation technique into a flask containing a solution of allyl benzoate (**1a**, 162 mg, 1 mmol), tetrakis(triphenylphosphine)palladium (57.8 mg, 0.05 mmol), and chlorotrimethylsilane (508 μL, 4.0 mmol) in THF (5 mL) under an atmosphere of carbon monoxide (a balloon). The mixture was stirred at room temperature for 30 h and worked up as shown in case 1 to provide ethyl 5-oxo-7-octenoate (**6a**, R_f = 0.4, hexane:ethyl acetate 4:1, v/v) in 78% yield. **Attempted Deuterium Incorporation into a Presumable Intermediate, Ethyl 5-(Trimethylsiloxy)-5,7-octadienoate (Scheme 1).** After completion of the above-mentioned reaction, 2 N DCl in D_2O (2 mL) was added into the mixture via a syringe, and the resultant mixture was stirred for 2 h at room temperature under N_2 and then diluted with ethyl acetate (70 mL) and washed with 1 N HCl (2 × 10 mL), saturated $NaHCO_3$, and brine. The ^1H NMR spectrum (400 MHz) of **6a**, purified by column chromatography over silica gel, showed no decrease in the area intensity of the allylic methylene protons (δ 3.17 ppm).

Case 4 (run 5, Table 4). A typical procedure for the reactions of zincio nitriles **9** and crotyl benzoate (**1b′**) in the presence of HMPA: A mixture of 7-iodoheptanenitrile (593 mg, 2.5 mmol), zinc–copper couple (247 mg, 3.75 mmol), and HMPA (1.97 mL, 11.3 mmol) in THF (5 mL) was refluxed for 3 h under N_2. After being allowed to cool, the mixture was transferred by cannulation technique into a flask containing a solution of crotyl benzoate (**1b′**, 176 mg, 1 mmol) and tetrakis(triphenylphosphine)palladium (57.8 mg, 0.05 mmol) in THF (5 mL) under an atmosphere of carbon monoxide (a balloon). The mixture was stirred at room temperature for 20 h. After dilution with ethyl acetate (70 mL), the mixture was washed successively with 1 N HCl (2 × 10 mL), saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by column chromatography over silica gel (benzene as a eluent) to give 8-oxo-10-dodecenenitrile (**10e**, as a mixture of *cis* and *trans* isomers in a ratio of 36:64, R_f = 0.20, benzene:ethyl acetate = 32:1, v/v) and 9-methyl-8-oxo-10-undecenenitrile (**11e**, R_f = 0.26) in 44 and 40% yields, respectively.

Case 5 (run 1, Table 5). A typical procedure for the reactions of octylzinc iodide and allylic benzoates **1** in the presence of HMPA. Determination of regioselectivity for the carbonylation with unsymmetrical allylating agents: A mixture of octyl iodide (600 mg, 2.5 mmol), zinc–copper couple (247 mg, 3.75 mmol), and HMPA (1.97 mL, 11.3 mmol) in THF (5 mL) was refluxed for 3 h under N_2 with well stirring. After being allowed to cool, the mixture was transferred by cannulation technique into a flask containing a solution of crotyl benzoate (**1b′**, 176 mg, 1 mmol) and tetrakis(triphenylphosphine)palladium (57.8 mg, 0.05 mmol) in THF (5 mL), purged with carbon monoxide (a balloon). The mixture was stirred at room temperature for 26 h and then poured into ethyl acetate (70 mL). Usual workup as indicated in case 1, followed by column chromatography over silica gel, provided crotyl octyl ketone (R_f = 0.60, hexane:ethyl acetate = 4:1, as a mixture of *cis*:*trans* = 32:68) and α-methylallyl octyl ketone (R_f = 0.68) in 40 and 42% yields, respectively.

Case 6 (run 7, Table 5). A typical procedure for the reactions of diethylzinc and allylic phosphates in the presence of HMPA: A 25 mL two-necked round-bottomed flask containing tetrakis(triphenylphosphine)palladium (57.8 mg, 0.05 mmol) and a stirring bar was fitted with a serum cap and a reflux condenser equipped at the top with a three-way stopcock connected with a balloon filled with carbon monoxide. Into this flask were added successively diethyl perillyl phosphate (**1f′**, 244 mg, 1 mmol, dissolved in 5 mL of THF), HMPA (1.97 mL, 11.3 mmol), and diethylzinc (1.5 M THF solution, 1 mL). The mixture was stirred at room temperature for 40 h under 1 atm of carbon monoxide (a balloon) and then poured into 2 N HCl (10 mL). After usual workup, as indicated in case 1, ethyl perillyl ketone (R_f = 0.61, hexane:ethyl acetate = 4:1, v/v) was isolated as a colorless liquid in 48% yield. The reaction of run 6 in Table 5 provided the same ketone in 52% yield together with the recovered **1f′** (R_f = 0.1, 14%).

Case 7 (eq 5). A typical procedure for the reactions of γ-zincio ester **5**, free from HMPA, and allylic benzoates **1**: Ethyl γ-zinciobutyrate **5** (0.5 M solution in THF), free from HMPA, was prepared according to the literature,[34] and the supernatant solution (5 mL) was introduced via a syringe into a solution of allyl benzoate (**1a**, 1 mmol) and tetrakis(triphenylphosphine)palladium (57.8 mg, 0.05 mmol) in THF (5 mL). The mixture was stirred under 1 atm of carbon monoxide (a balloon) at room temperature for 6 h. After usual workup, as indicated in case 1, the residue was subjected to column chromatography over silica gel to afford ethyl 5-oxo-7-octenoate (**6a**, R_f = 0.4, hexane:ethyl acetate = 4:1, v/v), δ,δ-diallyl δ-valerolactone (**12b**, R_f = 0.29), diethyl 5-oxoazelate (**14b**, R_f = 0.19), δ-allyl-δ-(3-ethoxycarbonylpropyl) δ-valerolactone (**13b**, R_f = 0.11) in 14, 9, 14, and 36% yields, respectively.

Case 8 (second column, Scheme 5). A typical procedure for the reactions of β-zincio ester **2** and allylic benzoates **1** in the presence of HMPA and benzaldehyde: A solution of **2** (2.5 mmol) in HMPA (11.3 mmol) and THF (5 mL) was prepared as usual (case 1). This solution was transferred by cannulation technique into a flask containing a solution of allyl benzoate (**1a**, 162 mg, 1 mmol), benzaldehyde (106 mg, 1 mmol), and tetrakis(triphenylphosphine)palladium (57.8 mg, 0.05 mmol) in THF (5 mL) under an atmosphere of carbon monoxide (a balloon). The mixture was stirred at room temperature for 40 h. After addition of 1 N HCl (10 mL), the mixture was extracted with ethyl actate (3 × 25 mL), and the combined extracts were washed successively with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by column chromatography over silica gel (benzene:ethyl acetate = 32:1, v/v) to give diethyl 4-oxopimelate (**14a**, R_f = 0.08, benzene:ethyl acetate = 32:1, v/v, 60% yield, based on **1a**) and a mixture of ethyl 4-oxo-6-heptenoate (**3a**, R_f = 0.44, 20% yield) and 1-phenyl-3-buten-1-ol (R_f = 0.44, 42% yield), the ratio being determined by high-field ^1H NMR (400 MHz).

Case 9 (fourth column, Scheme 5). A typical procedure for the reactions of β-zincio ester **2**, free from HMPA, and allylic benzoates **1** in the presence of benzaldehyde: A solution of β-zincio ester **2** (2.5 mmol), free from HMPA, in THF (5 mL) was prepared according to the procedure indicated in case 2. This solution was transferred by cannulation technique into a flask containing a solution of allyl benzoate (**1a**, 162 mg, 1 mmol), benzaldehyde (212 mg, 2 mmol), and tetrakis(triphenylphosphine)palladium (57.8 mg, 0.05 mmol) in THF (5 mL). The mixture was stirred at room temperature for 20 h under 1 atm of carbon monoxide (a balloon). After usual extractive workup as case 8, the residue was purified by column chromatography over silica gel (benzene:ethyl acetate = 32:1, v/v) to give 1-phenyl-3-buten-1-ol (R_f = 0.44) and diethyl 4-oxopimelate (**14a**, R_f = 0.08, benzene:ethyl acetate = 32:1, v/v) in 80 and 87% yields (based on **1a**), respectively.

Case 10 (Scheme 7). A typical procedure for the reactions of γ-zincio ester **5** and allylic phosphates in the presence of HMPA. Determination of stereochemical course: A solution of γ-zincio ester **5** (5.0 mmol) in THF (10 mL) and HMPA (22.6

(34) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, *56*, 1445–1453.

mmol) was prepared according to the procedure indicated in case 1. This solution was transferred by cannulation technique into a flask containing a solution of *trans*-carvyl diethyl phosphate (*trans*-**1h**, 577 mg, 2 mmol, a crude extract prepared according to the procedure described above) and tetrakis-(triphenylphosphine)palladium (116 mg, 0.1 mmol) in THF (10 mL) under an atmosphere of carbon monoxide (a balloon). The mixture was stirred at room temperature for 72 h. After usual extractive workup as in case 8, the residue was purified by column chromatography over silica gel to give *cis*-carvyl γ-(ethoxycarbonyl)propyl ketone (*cis*-**6h**, R_f = 0.60, hexane: ethyl acetate = 4:1, v/v) in 59% yields. The stereochemical purity (100%) of *cis*-**6h** was confirmed by the comparison of the high-field ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra with those of a mixture of *trans*- and *cis*-**6h** (97:3), obtained by the similar reaction starting from a mixture of *cis*- and *trans*-carvyl phosphates (*cis*-**1h**:*trans*-**1h** = 98:2).

Physical and Spectral Data of the Products Listed in Table 1. Ethyl 4-oxo-6-heptenoate (3a): bp 104 °C/1.8 mmHg: IR (neat film) 2978 (m), 2930 (m), 1735 (s), 1710 (s), 1642 (w), 1372 (m), 1162 (s), 1091 (m), 1023 (m), 971 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 1.24 (t, J = 7.0 Hz, 3 H), 2.47–2.64 (m, 4 H), 3.14 (d, J = 6.2 Hz, 2 H), 4.08 (q, J = 7.0 Hz, 2 H), 4.93–5.24 (m, 2 H), 5.90 (m, 1 H); HRMS calcd for $C_{13}H_{14}O_3$ *m/e* 170.0943, found (relative intensity) 170.0937 (M^+, 2), 129 (100), 125 (66). Anal. Calcd for $C_{13}H_{14}O_3$: C, 63.51; H, 8.30. Found: C, 63.54; H, 8.24.

Ethyl 4-oxo-6-octenoate (3b): bp 120 °C/0.4 mmHg: IR (neat film) 2960 (w), 1725 (s), 1710 (s), 1631 (w), 1365 (m), 1183 (s), 1077 (m), 1022 (m), 958 (w), 912 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) (***trans* isomer**) δ 1.25 (t, J = 7.1 Hz, 3 H), 1.71 (br d, J = 4.8 Hz, 3 H), 2.57 (t, J = 6.6 Hz, 2 H), 2.75 (t, J = 6.6 Hz, 2 H), 3.15 (br d, J = 5.5 Hz, 2 H), 4.13 (q, J = 7.1 Hz, 2 H), 5.49–5.63 (m, 2 H); (***cis* isomer**) δ 1.25 (t, J = 7.1 Hz, 3 H), 1.65 (br d, J = 6.6 Hz, 3 H), 2.59 (t, J = 5.9 Hz, 2 H), 2.77 (t, J = 5.9 Hz, 2 H), 3.23 (br d, J = 7.3 Hz, 2 H), 4.13 (q, J = 7.1 Hz, 2 H), 5.55 (m, 1 H), 5.70 (dm, J = 10.8 Hz, 1 H). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.07; H, 8.68.

Ethyl 6-methyl-4-oxo-6-heptenoate (3c): bp 100 °C/0.4 mmHg: IR (neat film) 3078 (w), 2980 (m), 1736 (s), 1720 (s), 1656 (w), 1377 (s), 1192 (s), 1098 (m), 1028 (m), 895 (m) cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) δ 1.24 (t, J = 7.0 Hz, 3 H), 1.74 (s, 3 H), 2.28–2.83 (m, 4 H), 3.07 (s, 2 H), 4.08 (q, J = 7.0 Hz, 2 H), 4.75–4.97 (m, 2 H). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.19; H, 8.75.

Ethyl 7-methyl-4-oxo-6-heptenoate (3d): bp 80 °C/0.08 mmHg: IR (neat film) 2960 (m), 1730 (s), 1711 (s), 1639 (w), 1365 (s), 1340 (m), 1174 (s), 1090 (m), 1018 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 1.22 (t, J = 7.2 Hz, 3 H), 1.66 (s, 3 H), 1.77 (s, 3 H), 2.30–2.83 (m, 4 H), 3.07 (d, J = 7.0 Hz, 2 H), 4.12 (q, J = 7.2 Hz, 2 H), 5.20 (m, 1 H). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.57; H, 9.06.

Ethyl 5,5-dimethyl-4-oxo-6-heptenoate (4d): IR (neat film) 3080 (w), 2976 (s), 2930 (m), 1730 (s), 1715 (s), 1640 (w), 1208 (s), 1177 (s), 1081 (m), 1013 (m), 920 (m) cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) δ 1.22 (s, 6 H), 1.26 (t, J = 7.2 Hz, 3 H), 2.21–2.91 (m, 4 H), 4.10 (q, J = 7.2 Hz, 2 H), 4.98–5.34 (m, 2 H), 6.00 (dd, J = 17.1, 10.0 Hz, 1 H); HRMS calcd for $C_{11}H_{18}O_3$ *m/e* 198.1256, found (relative intensity) 198.1224 (M, 0.1), 153 (28), 152 (3), 129 (100). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.67; H, 9.16.

Physical and Spectral Data of the Products Listed in Table 3. Ethyl 5-oxo-7-octenoate (6a): bp 107 °C/3.8 mmHg: IR (neat film) 2980 (m), 1728 (s), 1643 (w), 1085 (s), 1033 (m), 920 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.25 (t, J = 7.1 Hz, 3 H), 1.89 (quint, J = 7.3 Hz, 2 H), 2.32 (t, J = 7.3 Hz, 2 H), 2.53 (t, J = 7.3 Hz, 2 H), 3.17 (d, J = 7.0 Hz, 2 H), 4.12 (q, J = 7.1 Hz, 2 H), 5.10–5.20 (m, 2 H), 5.91 (ddt, J = 17.2, 10.3, 7.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 14.10, 18.07, 33.18, 40.96, 47.65, 60.23, 118.72, 130.40, 172.98, 207.62; HRMS calcd for $C_{10}H_{16}O_3$ *m/e* 184.1100, found (relative intensity) 184.1116 (M, 8), 139 (20), 111 (8), 69 (100).

Ethyl 5-oxo-6-vinyl-8-nonenoate (8a): bp 115 °C/0.5 mmHg: IR (neat film) 3080 (m), 1732 (s), 1650 (m), 1185 (m), 1032 (m), 920 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.25 (t, J = 7.1 Hz, 3 H), 1.87 (quint, J = 7.3 Hz, 2 H), 2.25 (m, 1 H, coalescing to dd, J = 13.8, 7.0 by irradiation at 5.70), 2.30 (t, J = 7.3 Hz, 1 H), 2.48 (dt, J = 17.6, 7.3 Hz, 1 H), 2.49 (m, 1 H), 2.60 (dt, J = 17.6, 7.3 Hz, 1 H), 3.18 (dt, J = 8.8, 7.0 Hz, 1 H), 4.12 (q, J = 7.1 Hz, 2 H), 4.98–5.07 (m, 2 H), 5.15–5.20 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ 14.2, 18.7, 33.3, 35.1, 40.4, 57.2, 60.3, 116.7, 118.2, 135.3, 135.8, 173.1, 209.5; HRMS calcd for $C_{13}H_{20}O_3$ *m/e* 224.1413, found (relative intensity) 224.1413 (M, 3), 179 (13), 143 (84), 115 (41), 69 (100).

Ethyl 5-oxo-7-nonenoate (6b): bp 85 °C/0.1 mmHg: IR (neat film) 2980 (s), 1740 (s), 1720 (s), 1445 (m), 1375 (m), 1185 (s), 1100 (m), 1035 (m) cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) δ 1.24 (t, J = 7.0 Hz, 3 H), 1.54–2.71 (m, 9 H), 2.95–3.23 (m, 2 H), 4.13 (q, J = 7.0 Hz, 2 H), 5.20–5.87 (m, 2 H); HRMS calcd for $C_{11}H_{18}O_3$ *m/e* 198.1256, found (relative intensity) 198.1248 (M, 9), 153 (62), 143 (149), 115 (100), 87 (66), 69 (75).

Ethyl 7-methyl-5-oxo-7-octenoate (6c): bp 85 °C/0.1 mmHg: IR (neat film) 2950 (m), 1730 (s), 1710 (s), 1440 (w), 1365 (m), 1180 (s), 1020 (m) cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) δ 1.25 (t, J = 7.0 Hz, 3 H), 1.50–2.75 (m, 6 H), 1.75 (br s, 3 H), 3.09 (s, 2 H), 4.13 (q, J = 7.0 Hz, 2 H), 4.77–5.00 (m, 2 H); HRMS calcd for $C_{11}H_{18}O_3$ *m/e* 198.1256, found (relative intensity) 198.1270 (M, 3), 153 (33), 143 (84), 125 (20), 69 (100). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.60; H, 9.18.

Ethyl 8-methyl-5-oxo-7-nonenoate (6d): bp 95 °C/0.15 mmHg; IR (neat film) 2976 (s), 1730 (s), 1718 (s), 1448 (m), 1180 (s), 1113 (m), 1099 (m), 1030 (m), 920 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.23 (t, J = 7.3 Hz, 3 H), 1.63 (s, 3 H), 1.75 (s, 3 H), 1.89 (quint, J = 7.3 Hz, 2 H), 2.32 (t, J = 7.3 Hz, 2 H), 2.50 (t, J = 7.3 Hz, 2 Hz), 3.10 (d, J = 7.3 Hz, 2 H), 4.12 (q, J = 7.3 Hz, 2 H), 5.28 (br d, J = 7.3 Hz, 1 H); HRMS calcd for $C_{12}H_{20}O_3$ *m/e* 212.1413, found (relative intensity) 212.1405 (M, 23), 167 (32), 143 (100).

Ethyl 6,6-dimethyl-5-oxo-7-octenoate (7d): bp 86 °C/0.3 mmHg: IR (neat film) 3076 (w), 2966 (s), 1730 (s), 1710 (s), 1640 (m), 1370 (s), 1245 (s), 1179 (s), 1092 (m), 1030 (m), 919 (m) cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) δ 1.20 (s, 6 H), 1.23 (t, J = 7.0 Hz, 3 H), 1.50–2.00 (m, 2 H), 2.03–2.62 (m, 4 H), 4.07 (q, J = 7.0 Hz, 2 H), 4.87–5.25 (m, 2 H), 5.90 (dd, J = 17.8, 9.6 Hz, 1 H). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.53; H, 9.50.

Ethyl 5-oxo-8-phenyl-7-octenoate (6e): bp 120 °C/0.15 mmHg: IR (neat film) 3059 (w), 2979 (m), 2935 (m), 1730 (s), 1715 (s), 1371 (m), 1180 (s), 1026 (m), 962 (w), 918 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.24 (t, J = 7.1 Hz, 3 H), 1.91 (quint, J = 7.3 Hz, 2 H), 2.33 (t, J = 7.3 Hz, 2 H), 2.57 (t, J = 7.3 Hz, 2 H), 3.31 (d, J = 7.1 Hz, 2 H), 4.10 (q, J = 7.1 Hz, 2 H), 6.29 (dt, J = 7.1 Hz, 1 H), 6.47 (d, J = 15.8 Hz, 1 H), 7.03 (m, 5 H); HRMS calcd for $C_{16}H_{20}O_3$ *m/e* 260.1412, found (relative intensity) 260.1421 (M, 17), 215 (10), 157 (28), 128 (26), 115 (100).

Ethyl 5-oxo-6-phenyl-7-octenoate (7e): bp 120 °C/0.15 mmHg: IR (neat film) 3082 (w), 2980 (m), 1735 (s), 1720 (s), 1645 (w), 1376 (m), 1250 (m), 1183 (s), 1096 (m), 1031 (m), 992 (w), 922 (m) cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) δ 1.19 (t, J = 7.0 Hz, 3 H), 1.43–2.62 (m, 6 H), 4.02 (q, J = 7.0 Hz, 2 H), 4.27 (d, J = 8.0 Hz, 1 H), 4.79–5.29 (m, 2 H), 6.18 (ddd, J = 17.0, 10.0, 8.0 Hz, 1 H), 7.02–7.44 (m, 5 H). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.94; H, 7.79.

Ethyl 5-oxo-9-phenyl-6-(β-styryl)-8-nonenoate (8e): IR (neat film) 3024 (m), 2978 (m), 1730 (s), 1715 (s), 1672 (w), 1600 (w), 1376 (m), 1182 (m), 1160 (m), 1030 (m), 968 (m), 920 (w), 749 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.19 (t, J = 7.1 Hz, 3 H), 1.89 (quint, J = 7.1 Hz, 1 H), 1.90 (quint, J = 7.1 Hz, 1 H), 2.29 (t, J = 7.1 Hz, 2 H), 2.45–2.58 (m, 2 H), 2.62–2.77 (m, 2 H), 3.41 (dt, J = 9.0, 7.1 Hz, 1 H), 4.06 (q, J = 7.1 Hz, 2 H), 6.12 (dd, J = 15.8, 9.0 Hz, 1 H), 6.13 (dt, J = 15.8, 7.1 Hz, 1H), 6.43 (d, J = 15.8 Hz, 1 H), 6.54 (d, J = 15.8 Hz, 1 H), 7.10–7.40 (m, 10 H); HRMS calcd for $C_{25}H_{28}O_3$ *m/e* 376.2039, found (relative intensity) 376.2046 (M, 8), 277 (7), 215 (8), 129 (7), 118 (100).

Ethyl 5-(2-cyclohexenyl)-5-oxopentanoate (6g): bp 92 °C/0.37 mmHg: IR (neat film) 2980 (m), 2938 (s), 1737 (s), 1670 (s), 1648 (m), 1378 (m), 1202 (s), 1100 (w), 1030 (m), 992 (m) cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) 1.23 (t, J = 7.0 Hz, 3 H), 1.50–2.65 (m, 12 H), 2.95 (m, 1 H), 4.08 (q, J = 7.0 Hz, 2 H), 5.68–5.83 (m, 2 H); HRMS calcd for $C_{13}H_{20}O_3$ *m/e* 224.1412, found

(relative intensity) 224.1422 (M, 64), 179 (66), 178 (93), 109 (100), 81 (29).

Physical and Spectral Data of the Products Listed in Table 4. 4-Oxo-6-octenenitrile (10a): mixture of *cis* and *trans* isomers, the ratio not determined; bp 98 °C/0.4 mmHg; IR (neat film) 3036 (w), 2940 (m), 2256 (m), 1720 (s), 1672 (m), 1417 (m), 1380 (m), 1088 (m), 970 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (***trans* isomer**) δ 1.72 (dm, J = 6.7, ca. 1.0 Hz, 3 H), 2.57 (t, J = 7.3 Hz, 2 H), 2.84 (t, J = 7.3, 2 H), 3.14 (br d, J = 6.6 Hz, 2 H), 5.46–5.67 (m, 2 H); (***cis* isomer**) δ 1.66 (dm, J = 6.7, ca. 1.0 Hz, 3 H), 2.59 (t, J = 7.1 Hz, 2 H), 2.85 (t, J = 7.1 Hz, 2 H), 3.22 (br d, J = 7.3 Hz, 2 H), 5.57 (m, 1 H), 5.75 (m, 1 H). Anal. Calcd for $C_8H_{11}NO$: C, 70.05; H, 8.08; N, 10.21. Found: C, 69.76; H, 8.04; N, 10.01.

5-Oxo-7-nonenenitrile (10b): mixture of *cis*:*trans* = 28:72; bp 105 °C/0.3 mmHg; IR (neat film) 3020 (w), 2938 (w), 2240 (w), 1715 (s), 1454 (w), 1093 (w), 969 (m) cm^{-1}; ^1H NMR ($CDCl_3$ 400 MHz) (***trans* isomer**) δ 1.72 (br d, J = 5.9 Hz, 3 H), 1.92 (quint, J = 7.0 Hz, 2 H), 2.42 (t, J = 7.0 Hz, 2 H), 2.64 (t, J = 7.0 Hz, 2 H), 3.11 (br d, J = 6.6 Hz, 2 H), 5.52–5.64 [(m, 2 H, coalescing to 5.59 (d, J = 15.2) and 5.52 (dt, J = 15.2, 6.6 Hz) by irradiation at 1.72]; (***cis* isomer**) δ 1.66 (br d, J = 7.7 Hz, 3 H), 1.93 (quint, J = 7.0 Hz, 2 H), 2.43 (t, J = 7.0 Hz, 2 H), 2.66 (t, J = 7.0 Hz, 2 H), 3.20 (br d, J = 7.3 Hz, 2 H), 5.56 (m, 1 H), 5.72 (m, 1 H, coalescing to br d, J = 11.0 Hz by irradiation at 1.66); HRMS calcd for $C_9H_{13}NO$ *m/e* 151.0997, found (relative intensity) 151.1012 (M, 31), 96 (100), 83 (8), 69 (21), 68 (35).

6-Oxo-8-decenenitrile (10c): mixture of *cis* and *trans* isomers, the ratio not determined; bp 98 °C/0.03 mmHg; IR (neat film) 3036 (w), 2940 (s), 2250 (m), 1717 (s), 1670 (m), 1452 (m), 1380 (m), 1116 (w), 1096 (w), 1038 (w), 969 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (***trans* isomer**) δ 1.62–1.79 (m, 7 H), 2.35 (t, J = 6.8 Hz, 2 H), 2.50 (t, J = 6.8 Hz, 2 H), 3.09 (br d, J = 6.6 Hz, 2 H), 5.47–5.62 (m, 2 H); (***cis* isomer**) δ 1.62–1.79 (m, 7 H), 2.36 (t, J = 6.8 Hz, 2 H), 2.51 (t, J = 6.8 Hz, 2 H), 3.17 (br d, J = 7.3 Hz, 2 H), 5.55 (m, 1 H), 5.70 (m, 1H). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.49; H, 9.10; N, 8.17.

7-Oxo-9-undecenenitrile (10d): mixture of *cis*:*trans* = 28:72; bp 130 °C/0.03 mmHg; IR (neat film) 3032 (w), 2938 (s), 2868 (m), 2250 (m), 1717 (s), 1373 (m), 1269 (w), 1100 (w), 968 (m), 913 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (***trans* isomer**) 1.40–1.49 (m, 2 H), 1.56–1.72 (m, 7 H), 2.35 (t, J = 7.1 Hz, 2 H), 2.46 (t, J = 7.1 Hz, 2 H), 3.09 (br d, J = 5.9 Hz, 2 H), 5.48–5.60 (m, 2 H); (***cis* isomer**) 1.40–1.49 (m, 2 H), 1.56–1.72 (m, 7 H), 2.35 (t, J = 7.1 Hz, 2 H), 2.48 (t, J = 6.8 Hz, 2 H), 3.17 (br d, J = 7.3 Hz, 2 H), 5.58 (m, 1 H), 5.70 (m, 1 H, coalescing to dq, J = 10.8, 6.8 Hz by irradiation at 3.17). Anal. Calcd for $C_{11}H_{17}ON$: C, 73.70; H, 9.56; N, 7.81. Found: 73.51; H, 9.64; N, 7.64.

8-Oxo-10-dodecenenitrile (10e): mixture of *cis*:*trans* = 36:64; bp 105 °C/0.04 mmHg; IR (neat film) 3030 (w), 2938 (s), 2244 (w), 1718 (s), 1372 (m), 1211 (w), 1105 (w), 1078 (w), 1058 (w), 969 (m), 922 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (***trans* isomer**) δ 1.28–1.37 (m, 2 H), 1.42–1.50 (m, 2 H), 1.54–1.72 (m, 7 H), 2.34 (t, J = 7.1 Hz, 2 H), 2.44 (t, J = 7.1 Hz, 2 H), 3.09 (br d, J = 5.5 Hz, 2 H), 5.48–5.60 (m, 2 H); (***cis* isomer**) 1.28–1.37 (m, 2 H), 1.42–1.50 (m, 2 H), 1.54–1.72 (m, 7 H), 2.34 (t, J = 7.1 Hz, 2 H), 2.46 (t, J = 7.1 Hz, 2 H), 3.17 (d, J = 7.1 Hz, 2 H), 5.56 (m, 1 H), 5.69 (m, 1 H, coalescing to dq, J = 11.0, 6.0 Hz by irradiation at 3.17); HRMS calcd for $C_{12}H_{19}NO$ *m/e* 193.1467, found (relative intensity) 193.1453 (M, 15), 138 (100), 110 (57), 69 (54).

7-Methyl-6-oxo-8-nonenenitrile (11c): bp 98 °C/0.04 mmHg; IR (neat film) 3074 (w), 1710 (s), 1640 (m), 1371 (m), 1170 (w), 1118 (w), 1091 (w), 996 (m), 920 (m) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.15 (d, J = 7.0 Hz, 3 H), 1.43–1.83 (m, 4 H), 2.13–2.63 (m, 4 H), 3.13 (quint, J = 7.0 Hz, 1 H), 4.93–5.30 (m, 2 H), 5.83 (ddd, J = 17.6, 9.0, 7.0 Hz, 1 H). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 9.68. Found: C, 72.40; H, 9.22; N, 8.38.

8-Methyl-7-oxo-9-dodecenenitrile (11d): bp 130 °C/0.03 mmHg; IR (neat film) 3080 (w), 2242 (m), 1711 (s), 1641 (m), 1372 (m), 1268 (w), 1116 (w), 1000 (m), 911 (m) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.10 (d, J = 7.0 Hz, 3 H), 1.28–1.97 (m, 6H), 2.03–2.62 (m, 4 H), 3.08 (quint, J = 7.0 Hz, 1 H), 4.90–5.28 (m, 2 H), 5.77 (ddd, J = 17.0, 9.0, 7.0 Hz, 1 H). Anal. Calcd for $C_{14}H_{17}NO$: C, 73.70; H, 9.56; N, 8.93. Found: C, 73.32; H, 9.66; N, 7.72.

9-Methyl-8-oxo-10-undecenenitrile (11e): bp 90 °C/0.03 mmHg; IR (neat film) 3076 (w), 2240 (m), 1710 (s), 1640 (m), 1370 (m), 1117 (w), 1022 (w), 996 (m), 920 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.18 (d, J = 7.0 Hz, 3 H), 1.25–1.36 (m, 2 H), 1.41–1.51 (m, 2 H), 1.53–1.71 (m, 4 H), 2.34 (t, J = 7.0 Hz, 2 H), 2.44 (dt, J = 17.4, 7.1 Hz, 1 H), 2.53 (dt, J = 17.4, 7.1 Hz, 1 H), 3.20 (dq, J = 7.0, 7.9 Hz, 1 H), 5.12–5.21 (m, 2 H), 5.80 (ddd, J = 17.2, 9.9, 7.9 Hz, 1 H); HRMS calcd for $C_{12}H_{19}NO$ *m/e* 193.1467, found (relative intensity) 193.1467 (M^+, 8), 138 (100), 110 (51), 69 (33).

Physical and Spectral Data of the Products Listed in Table 5. 2-Butenyl octyl ketone (a mixture of cis:trans = 32:68): bp 85 °C/2.8 mmHg; IR (neat film) 3030 (w), 2922 (s), 1720 (s), 1372 (w), 1130 (w), 1080 (w), 978 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (***trans* isomer**) δ 0.88 (t, J = 7.0 Hz, 3 H), 1.27–1.31 (m, 10 H), 1.52–1.60 (m, 2 H), 1.71 (br d, J = 7.3 Hz, 2 H), 3.07–3.10 (m, 2 H), 5.48–5.58 (m, 2 H); (***cis* isomer**) δ 0.88 (t, J = 7.0 Hz, 3 H), 1.27–1.31 (m, 10 H), 1.52–1.60 (m, 2 H), 1.64 (br d, J = 6.6 Hz, 3 H), 2.43 (t, J = 7.3 Hz, 2 H), 3.16 (d, J = 7.3 Hz, 2 H), 5.67 (m, 1 H, coalescing to dt, J = 9.2, 1.1 Hz by irradiation at 1.64). Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: 79.40; H, 12.33.

1-Methyl-2-propenyl octyl ketone: bp 77 °C/2.8 mmHg; IR (neat film) 3076 (w), 2958 (s), 1717 (s), 1644 (w), 1372 (m), 1130 (w), 996 (m), 916 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (br t, 3 H), 1.18 (d, J = 7.0 Hz, 3 H), 1.20–1.35 (m, 10 H), 1.50–1.60 (m, 2 H), 2.42 (dt, J = 16.9, 7.5 Hz, 1 H), 2.50 (dt, J = 16.9, 7.5 Hz, 1 H), 3.21 (dq, J = 7.9, 7.0 Hz, 1 H), 5.11–5.18 (m, 2 H), 5.81 (ddd, J = 17.2, 10.3, 8.1 Hz, 1 H). Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.58; H, 12.38.

3-Methyl-2-butenyl octyl ketone: bp 120 °C/0.18 mmHg; IR (neat film) 2932 (s), 1718 (s), 1378 (m), 1140 (w), 1077 (w), 980 (w) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 0.72–1.03 (m, 3 H), 1.07–1.53 (m, 12 H), 1.63 (s, 3 H), 1.75 (s, 3 H), 2.10–2.50 (m, 2 H), 2.97 (d, J = 7.0 Hz, 2 H), 5.23 (tm, J = 7.0 Hz, 1 H); HRMS calcd for $C_{14}H_{26}O$ *m/e* 210.1984, found (relative intensity) 210.1979 (24), 141 (100), 123 (5), 71 (20). Anal. Calcd for $C_{14}H_{26}O$: C, 79.94; H, 12.46. Found: C, 79.80; H, 12.55.

1,1-Dimethyl-2-propenyl octyl ketone: bp 80 °C/1.1 mmHg; IR (neat film) 3082 (w), 2960 (s), 1715 (s), 1645 (w), 1380 (m), 1122 (w), 1070 (m), 996 (m), 917 (m) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 0.67–1.74 (m, 21 H), 2.14–2.55 (m, 2 H), 4.88–5.30 (m, 2 H), 5.90 (dd, J = 17.6, 9.8 Hz, 1H). Anal. Calcd for $C_{14}H_{26}O$: C, 79.94; H, 12.46. Found: C, 79.91; H, 12.51.

***trans*-Cinnamyl octyl ketone**: bp 135 °C/0.12 mmHg; IR (neat film) 3060 (w), 2924 (s), 2854 (s), 1718 (s), 1681 (m), 1371 (w), 1070 (w), 1028 (w), 961 (m), 754 (m), 689 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87 (t, J = 7.0 Hz, 3 H), 1.22–1.32 (m, 10 H), 1.54–1.64 (m, 2 H), 2.48 (t, J = 7.5 Hz, 2 H), 3.32 (d, J = 7.1 Hz, 2 H), 6.31 (dt, J = 16.1, 7.1 Hz, 1 H), 6.47 (d, J = 16.1 Hz, 1 H), 7.20–7.41 (m, 5 H); HRMS calcd for $C_{18}H_{26}O$ *m/e* 258.1984, found (relative intensity) 258.1987 (M, 43), 160 (33), 117 (33), 68 (100).

1-Phenyl-2-propenyl octyl ketone: bp 95 °C/0.01 mmHg; IR (neat film) 3050 (w), 3022 (w), 2920 (s), 2850 (s), 1714 (s), 1640 (w), 1365 (m), 1072 (w), 1030 (w), 988 (m), 918 (m) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 0.63–1.73 (m, 15 H), 2.13–2.53 (m, 2 H), 4.24 (d, J = 7.6 Hz, 1 H), 4.79–5.27 (m, 2 H), 6.22 (ddd, J = 17.0, 10.2, 7.6 Hz, 1 H), 7.03–7.40 (m, 5 H); HRMS calcd for $C_{18}H_{26}O$ *m/e* 258.1984, found (relative intensity) 258.1981 (M, 30), 141 (100), 117 (23), 71 (19).

***trans*-1-(*trans*-β-Styryl)-4-phenyl-3-butenyl octyl ketone**: IR (neat film) 3060 (w), 3030 (w), 2926 (s), 1715 (s), 1600 (w), 1070 (w), 1030 (w), 963 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.85 (t, J = 7.0 Hz, 3 H), 1.15–1.30 (m, 10 H), 1.52–1.61 (m, 2 H), 2.36–2.53 (m, 2 H), 2.56 (dt, J = 17.2, 7.3 Hz, 1 H), 2.74 (m, 1 H), 3.42 (dt, J = 9.2, 6.6 Hz, 1 H), 6.13 (dd, J = 15.8, 9.2 Hz, 1 H), 6.14 (dt, J = 15.8, 7.3 Hz, 1 H), 6.43 (d, J = 15.8 Hz, 1 H), 6.54 (d, J = 15.8 Hz, 1 H), 7.12–7.39 (m, 10 H); HRMS calcd for $C_{27}H_{34}O$ *m/e* 374.2610, found (relative intensity) 374.2615 (M, 32), 257 (23), 141 (12), 117

(44), 69 (100). Anal. Calcd for $C_{27}H_{34}O$: C, 86.58; H, 9.15. Found: C, 86.33; H, 9.18.

Ethyl perillyl ketone: bp 105 °C/0.9 mmHg; IR (neat film) 3080 (w), 2920 (s), 1718 (s), 1670 (w), 1652 (m), 1350 (m), 1142 (w), 1038 (w), 970 (w), 946 (w), 917 (w) cm^{-1}; ^1H NMR ($CDCl_4$, 60 MHz) δ 0.99 (t, J = 7.2 Hz, 3 H), 1.19–2.20 (m, 10 H), 2.38 (q, J = 7.2 Hz, 2 H), 2.93 (s, 2 H), 4.68 (br s, 2 H), 5.50 (m, 1 H). Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.91; H, 10.49.

Physical and Spectral Data for the Products Listed in Scheme 3. γ,γ-Diallyl-γ-butyrolactone (12a): 110 °C/0.41 mmHg; IR (neat film) 3278 (w), 2980 (m), 1776 (s), 1735 (m), 1650 (w), 1189 (s), 1150 (m), 1022 (m), 998 (m), 920 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.07 (dd, J = 8.9, 8.0 Hz, 2 H), 2.40 (ddm, J = 14.3, 7.2 Hz, 2 H), 2.46 (ddm, J = 14.3, 7.2 Hz, 2 H), 2.56 (dd, J = 8.9, 8.0 Hz, 2 H), 5.15–5.21 (m, 2 H), 5.79 (ddt, J = 16.9, 10.3, 7.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) 29.01, 29.24, 43.57, 87.12, 119.93, 131.64, 176.60. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.12; H, 8.54.

δ,δ-Diallyl-δ-valerolactone (12b): bp 90 °C/0.1 mmHg; IR (neat film) 3076 (m), 2950 (m), 1730 (s), 1650 (m), 1337 (m), 1195 (w), 1032 (s), 1000 (m), 923 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.73–1.77 (m, 2 H, coalescing to br s by irradiation at 1.88), 1.82–1.94 (m, 2 H), 2.41 (br d, J = 7.0 Hz, 2 H), 2.43 (br d, J = 7.0 Hz, 2 H), 2.47 (t, J = 7.0 Hz, 2 H, coalescing to s by irradiation at 1.88), 5.11–5.20 (m, 4 H), 5.81 (ddt, J = 17.2, 10.1, 7.1 Hz, 2 H); HRMS calcd for $C_{11}H_{17}O_2$ *m/e* 181.1229, found (relative intensity) 181.1235 (M + 1, 12), 139.0764 (M − C_3H_5, 100).

γ-(2-Butenyl)-γ-(α-methylallyl)-γ-butyrolactone (12c): diastereomeric mixture of at least three isomers; bp 110 °C/0.05 mmHg; IR (neat film) 2970 (m), 2938 (m), 1774 (s), 1649 (w), 1420 (w), 1199 (m), 1016 (w), 973 (w), 930 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, only the characteristic absorptions) δ 1.06 (d, J = 6.6 Hz), 1.70 (d, J = 7.0 Hz), 1.08 (d, J = 6.2 Hz) [CH(CH_3)CH=CH_2], 1.64 (br d, J = 7.0 Hz), 1.69 (d, 6.2 Hz), [CH=CHCH_3], 1.90–2.62 (m, 7 H), 5.11–5.15 (m, 2 H), 5.34–5.88 (m, 3 H); HRMS calcd for $C_{12}H_{18}O_2$ *m/e* 194.1307, $C_{12}H_{19}O_2$ *m/e* 195.1385, found (relative intensity) 195.1404 (M + 1, 16), 194.1334 (M, 3), 139 (M − C_4H_7, 100), 121 (2), 111 (5), 97 (12).

γ-(2-Propenyl)-γ-(2-ethoxycarbonylethyl)-γ-butyrolactone (13a): bp 125 °C/0.4 mmHg; IR (neat film) 3078 (w), 2980 (m), 1780 (s), 1735 (s), 1650 (w), 1319 (s), 1181 (s), 1120 (m), 1101 (m), 1039 (m), 1005 (m), 941 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.26 (t, J = 7.2 Hz, 3 H), 1.95–2.05 (m, 3 H), 2.15 (dt, J = 13.2, 8.4 Hz, 1 H), 2.36–2.47 (m, 4 H), 2.59 (t, J = 8.6 Hz, 2 H), 4.14 (q, J = 7.2 Hz, 2 H), 5.18–5.22 (m, 2 H), 5.75 (ddm, J = 16.1, 11.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.07, 28.54, 28.78, 30.02, 33.84, 42.83, 60.61, 86.69, 120.20, 131.26, 172.67, 176.17. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.46; H, 8.05.

δ-Allyl-δ-[γ-(ethoxycarbonyl)propyl]-δ-valerolactone (13b): bp 160 °C/0.02 mmHg; IR (neat film) 3072 (w), 2950 (m), 1730 (s), 1651 (w), 1371 (m), 1240 (s), 1180 (s), 1060 (m), 1031 (m), 926 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.26 (t, J = 7.1 Hz, 3 H), 1.62–1.80 (m, 6 H), 1.80–1.92 (m, 2 H), 2.25–2.37 (m, 2 H), 2.37–2.45 (m, 2 H), 2.48 (t, J = 7.0 Hz, 2 H), 4.13 (q, J = 7.1 Hz, 2 H), 5.12–5.19 (m, 2 H), 5.78 (ddt, J = 17.6, 10.6, 7.1 Hz, 1 H). Anal. Calcd: C, 66.12; H, 8.72. Found: C, 65.97; H, 8.68.

Diethyl 4-oxopimelate (14a): bp 98 °C/0.025 mmHg; IR (neat film) 2979 (m), 2935 (w), 1731 (s), 1721 (s), 1372 (m), 1184 (s), 1101 (m), 1034 (m), 853 (w) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.26 (t, J = 7.2 Hz, 6 H), 2.30–2.88 (m, 8 H), 4.10 (q, J = 7.2 Hz, 4 H). Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.37; H, 7.82.

Diethyl 5-oxoazelate (14b): bp 140 °C/0.01 mmHg; IR (neat film) 2976 (m), 2938 (m), 1730 (s), 1715 (s), 1373 (s), 1311 (m), 1250 (s), 1180 (s), 1100 (m), 1079 (m), 1030 (m) cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.24 (t, J = 7.1 Hz, 6 H), 1.52–2.62 (m, 12 H), 4.05 (q, J = 7.1 Hz, 4 H); HRMS calcd for $C_{13}H_{22}O_5$ *m/e* 258.1467, found (relative intensity) 258.1467 (M, 21), 213 (47), 167 (60), 143 (100), 69 (24).

γ-(2-Butenyl)-γ-[δ-(ethoxycarbonyl)-β-oxo-α-(1-propenyl)butyl]-γ-butyrolactone (15): diastereomer mixture of at least four isomers; bp 168 °C/0.04 mmHg; IR (neat film) 2980 (m), 2942 (m), 1780 (s), 1738 (s), 1720 (s), 1450 (m), 1305 (m), 1260 (m), 1192 (s), 1021 (m), 975 (m), 936 (m), 912 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, only characterized absorptions) δ 1.24 (t, J = 7.1 Hz), 1.25 (t, J = 7.1 Hz), 1.26 (t, J = 7.1 Hz) [$CO_2CH_2CH_3$], 1.59–1.80 (m, 6 H), 1.81–2.63 (m, 8 H), 2.63–2.89 (m, 2 H), 3.52 (d, J = 9.5 Hz), 3.55 (d, J = 9.2 Hz), 3.59 (d, J = 9.9 Hz), 3.62 (d, J = 11.0 Hz) [CH(CO)-CH=$CHCH_3$], 5.34–5.96 (m, 4 H); MS *m/e* (relative intensity) 322 (M, 6), 267 (7), 164 (34), 139 (57), 129 (100), 101 (53). Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 66.87; H, 8.17.

Physical and Spectral Data for the Products Listed in Scheme 7. *cis*-Carvyl γ-(ethoxycarbonyl)propyl ketone (*cis*-6h): bp 105 °C/0.03 mmHg; IR (neat film) 3080 (w), 2972 (m), 2938 (s), 1732 (s), 1715 (s), 1670 (w), 1651 (m), 1311 (m), 1248 (m), 1176 (s), 1030 (m), 953 (w), 887 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.25 (t, 7.1 Hz, 3 H), 1.49 (q, J = 12 Hz, 3 H), 1.58 (br s, 3 H), 1.72 (s, 3 H), 1.84–2.02 (m, 4 H), 2.34 (t, J = 7.3 Hz, 2 H), 2.55 (t, J = 7.3 Hz, 2 H), 3.28 (m, 1 H), 4.13 (q, J = 7.1 Hz, 2 H), 4.71 (s, 1 H), 4.74 (br s, 1 H), 5.65 (m, 1 H); HRMS calcd for $C_{17}H_{26}O_3$ *m/e* 278.1882, found (relative intensity) 278.1884 (M, 19), 260 (4), 233 (16), 143 (100). Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41. Found: C, 73.04; H, 9.37.

***trans*-Carvyl γ-(ethoxycarbonyl)propyl ketone (*trans*-6h)**: bp 105 °C/0.03 mmHg; IR (neat film) 3070 (w), 2960 (s), 2922 (s), 1730 (s), 1712 (s), 1670 (w), 1652 (m), 1373 (m), 1247 (s), 1180 (s), 1100 (m), 1028 (m), 946 (w), 899 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.25 (t, J = 7.1 Hz, 3 H), 1.62 (br s, 3 H), 1.70 (s, 3 H), 1.75 (ddd, J = 13.6, 12.1, 6.8 Hz, 1 H), 1.82–2.00 (m, 4 H), 2.12–2.23 (m, 2 H), 2.33 (br, t, J = 7.3 Hz, 2 H), 2.51 (ddd, J = 17.2, 7.7, 6.6 Hz, 1 H), 2.67 (dt, J = 17.2, 7.3 Hz, 1 H), 3.11 (br d, J = 6.6 Hz, 1 H), 4.13 (q, J = 7.1 Hz, 2 H), 4.68 (br s, 1 H), 5.67 (m, 1 H); HRMS calcd for $C_{17}H_{26}O_3$ *m/e* 278.1882, found (relative intensity) 278.1883 (M, 12), 233 (18), 143 (100). Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.41. Found: C, 73.42; H, 9.43.

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Supplementary Material Available: ^1H NMR spectra for **6a**, **8a**, **6b**, **6d**, **6e**, **8e**, **6g**, **10b**, **10e**, **11e**, *trans*-cinnamyl octyl ketone, 1-phenyl-2-propenyl octyl ketone, **12b**, **12c**, **14b**, *cis*-**6h** (2D ^1H NMR), and *trans*-**6h** (2D ^1H NMR) (17 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.

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