JOC Article

Pd(0)-Catalyzed Conjugate Addition of Benzylzinc Chlorides to α,β-Enones in an Atmosphere of Carbon Monoxide: Preparation of 1,4-Diketones

Motoki Yuguchi, Masao Tokuda, and Kazuhiko Orito*

Laboratory of Organic Synthesis, Division of Molecular Chemistry Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan

orito@org-mc.eng.hokudai.ac.jp

Received October 7, 2003

Pd(0)-catalyzed conjugate addition of benzylzinc chloride to methyl vinyl ketone in the presence of chlorotrimethylsilane and lithium chloride in an atmosphere of carbon monoxide at room temperature afforded 1-phenyl-2,5-hexanedione monosilyl enol ether. In this catalytic carbonylation, four components are connected in one reaction. Successive acidic workup generated a variety of 1,4-diketones from substituted benzylzinc chlorides or related compounds and α,β-enones. Some products were converted to cyclopentenones or five-membered heterocyclic compounds containing an N, O, or S atom.

1,4-Diketones are useful synthetic precursors of substituted cyclopentenones and related compounds[1] such as jasmones,[2] rethorolones,[3] cuparenones,[4] and prostaglandins[5] and of five-membered heterocyclic compounds such as furans, thiophens, and pyrroles.[6] Methods for 1,4-acylation with masked acyl anions or their equivalents, such as thiazolinium salts, alkoxyvinylcuprates, cyanohydrin, nitronate anions, and anions of 1,3-dithians, have been studied for many years.[7] Conjugate additions of unmasked acyl anions [RCOM] such as acyllithium[8] or acyl-transition metal complexes (Fe,[9] Co,[10] Ni,[11] and Cu[12] complexes) to α,β-enones have also been reported. A Pd-catalyzed conjugate addition with acylzirconocene chlorides has been developed by Hanzawa and co-workers.[13] Radical carbonylation by interaction of an alkyl radical with α,β-enones in the presence of carbon monoxide has also been shown to afford 1,4-dicarbonyl compounds,[14] but a method with transition metal-catalyzed carbonylation has not been reported.

In a preceding work[15] we described copper-catalyzed conjugate addition of benzylzinc halides to α,β-enones in the presence of TMSCl.[16−19] This reaction produces a variety of 5-phenyl-2-pentanones. Further investigations revealed that when a Pd(0) catalyst was used in place of a copper catalyst under CO gas, carbonylation occurred in the reaction sequence to produce 1-phenyl-2,5-hexanediones. We report here a one-pot four-component connecting reaction for preparation of 1,4-diketones based

* Corresponding author.

(1) For reviews, see: (a) Ellison, R. A. *Synthesis*, **1973**, 387. (b) Piancattelli, G.; D'Auria, M.; D'Onofrio, F. *Synthesis* **1994**, 867.

(2) (a) For a review, see: Ho, T.-L. *Synth. Commun*. **1974**, *4*, 265. (b) Stetter, H.; Kulhmann, H. *Synthesis* **1975**, 379. (c) Tsukasa, H.; Saito, S. *Yukagaku* **1978**, *27*, 446. (d) Sun, P.-E.; Weiler, L. *Can. J. Chem*. **1978**, *56*, 2301. (e) Mussatto, M. C.; Savoia, D.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem*. **1980**, *45*, 4002. (f) Rao, A. V. R.; Deshpande, V. H.; Reddy, S. P. *Synth. Commun*. **1984**, *14*, 469. (g) Takahashi, K.; Aihara, T.; Ogura, K. *Chem. Lett*. **1987**, 2359. (h) Pecuniso, A.; Menicagli, R. *J. Org. Chem*. **1988**, *53*, 2614. (i) Fiandanese, V.; Marchese, G.; Naso, F. *Tetrahedron Lett*. **1988**, *29*, 3587. (j) Ballini, R.; Petrini, M. *Synth. Commun*. **1989**, *19*, 575. (k) Bergman, R.; Nilsson, B.; Wickberg, B. *Tetrahedron* **1990**, *31*, 2783. (l) Yamashita, M.; Tashika, H.; Uchida, M. *Bull. Chem. Soc. Jpn*. **1992**, *65*, 1257. (m) Tsukasa, H. *Biosci. Biotechnol. Biochem*. **1994**, *58*, 1181.

(3) Curran, D. P. *Tetrahedron Lett*. **1983**, *24*, 3443.

(4) (a) Wenkert, E.; Buckwalter, B. L.; Craveiro, A. A.; Sanchez, E. L.; Sathe, S. S. *J. Am. Chem. Soc*. **1978**, *100*, 1267. (b) Kametani, T.; Tubuki, A.; Nemoto, H. *Heterocycles* **1979**, *12*, 791. (c) Wenkert, E.; Greenberg, R. S.; Ragu, M. S. *J. Org. Chem*. **1985**, *50*, 4681.

(5) For reviews, see: (a) Bentley, P. H. *Chem. Soc. Rev*. **1974**, 29. (b) Mitra, A. *The Synthesis of Prostaglandins*; Wiley: New York, 1977. (c) Bindra, J. S.; Bindra, R. *Prostaglandin Synthesis*; Academic Press: New York, 1977. (d) Roberts, S. M.; Santoro, M. G.; Sickle *J. Chem. Soc., Perkin Trans. 1* **2002**, 1735.

(6) For reviews, see: (a) In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Cheeseman, G. W. H., Eds.; Pergamon Press: New York, 1984; Vol. 4. (b) Ferreira, V. F.; de Sousa, M. C. B. V.; Cunha, A. C.; Pereira, L. O. R.; Ferreira, M. L. G. *Org. Prep. Proced. Int*. **2001**, *33*, 4155.

(7) For a review on masked acyl anions, see: (a) Gröbel, B. T.; Seebach, D. *Synthesis* **1977**, 357. (b) Lever, O. W., Jr. *Tetrahedron* **1971**, *32*, 1943. (c) Albright, J. D. *Tetrahedron* **1983**, *39*, 3207.

(8) With RCOLi, see: Seyferth, D.; Hui, R. C. *J. Am. Chem. Soc*. **1985**, *107*, 4551.

(9) With RCOFe, see: (a) Cooke, M. P., Jr.; Parlman, R. M. *J. Am. Chem. Soc*. **1977**, *99*, 5222. (b) Yamashita, M.; Tashika, H.; Uchida, M. *Bull. Chem. Soc. Jpn*. **1992**, *65*, 1257.

(10) With RCOCo, see: Hegedus, L. S.; Perry, R. J. *J. Org. Chem*. **1985**, *50*, 4955.

(11) With RCONi, see: (a) Corey, E. J.; Hegedus, L. S. *J. Am. Chem. Soc*. **1969**, *91*, 4926. (b) Hermanson, J. R.; Hershberger, J. W.; Pinhas, A. R. *Organometallics* **1995**, *14*, 5426.

(12) With RCOCu(CN)Li, see: (a) Seyferth, D.; Hui, R. C. *Tetrahedron Lett*. **1986**, *27*, 1473. (b) Lipshutz, B. H.; Elworthy, T. R. *Tetrahedron Lett*. **1990**, *31*, 477. (c) Li, N.-S.; Yu, S.; Kabalka, G. W. *Organometallics* **1998**, *17*, 3815 and ref 8.

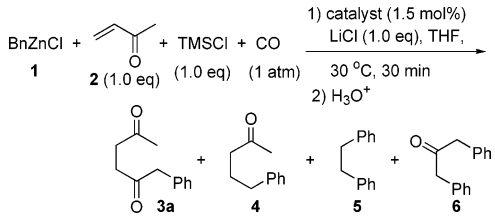
(13) With RCOZr and Pd catalyst, see: (a) Hanzawa, Y.; Tabuchi, N.; Taguchi, T. *Tetrahedron Lett*. **1998**, *39*, 8141. (b) Hanzawa, Y.; Tabuchi, N.; Narita, K.; Kakuuchi, A.; Yabe, M.; Taguchi, T. *Tetrahedron* **2002**, *58*, 7559.

(14) (a) Ryu, I.; Kusano, K.; Yamazaki, H.; Sonoda, N. *J. Org. Chem*. **1991**, *56*, 5003. (b) Ryu, I.; Yamazaki, H.; Ogawa, A.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc*. **1993**, *115*, 1187. (c) Kishimoto, Y.; Ikariya, T. *J. Org. Chem*. **2000**, *65*, 7656.

(15) Nishimura, T.; Yuguchi, M. Japanese Patent 226310, 2001; *Chem. Abstr*. **2001**, *135*, 180617.

10.1021/jo035468+ CCC: $27.50
Published on Web 01/13/2004

TABLE 1. Preparation of 1-Phenyl-2,5-hexanedione by Catalytic Carbonylation



		product yields[a] (%)			
entry	catalyst	**3a**	**4**	**5**	**6**
1		0	51	2	0
2	CuCl	0	64	3	1
3	$Pd(PPh_3)_4$	40	8	0	1
4	$PdCl_2$	0	26	7	9
5	$Pd_2(dba)_3$	7	8	1	28
6	$Pd_2(dba)_3 + 4PPh_3$	42	4	0	9
7	$Pd_2(dba)_3 + 4PBu_3$	27	4	1	13
8	$Pd(dppe)_2$	42	8	1	8
9	$Pd(OAc)_2 + 5PPh_3$	36	7	0	8
10	10% Pd/C	4	8	4	21
11	$Ni(PPh_3)_4$	0	23	6	0
12	$Pt(PPh_3)_4$	0	23	8	1
13	$Co_2(CO)_8$	2	21	1	2

[a] Determined by GC analysis.

on a TMSCl-assisted Pd(0)-catalyzed carbonylative conjugate addition of benzylzinc chloride to α,*β*-unsaturated ketones.

Benzylzinc chloride **1** was treated with methyl vinyl ketone (**2**, 1.0 equiv), TMSCl (1.0 equiv), and a Pd catalyst (1.5 mol %) in the presence of LiCl (1.0 equiv) in THF in an atmosphere of CO gas at 30 °C for 30 min. As shown in Table 1, the formation of non-carbonylated compound **4**, which was a main product in the above-mentioned CuC1-catalyzed coupling (entry 2),[15] was minimized by using a phosphine-ligated Pd(0) catalyst such as $Pd(PPh_3)_4$ or $Pd(dppe)_2$, and 1-phenyl-2,5-hexanedione (**3a**) was produced (entries 3, 6, 8, and 9). Pd(0) catalysts having no phosphine ligands and other metal catalysts were found to be not effective. In addition, this carbonylation occurred only on the *β*-carbon of the α,*β*-enones.

Further examinations were carried out with $Pd(PPh_3)_4$ as a catalyst (Table 2). Without TMSCl and LiCl, one-pot l,4-acylation did not occur (entries 3 and 5). The effect of LiCl was greater than that of NaCl. The use of 5 equiv of LiCl and 3.5 equiv of TMSCl and the slow addition of benzylzinc chloride over a period of 30 min resulted in the formation of the desired **3a** in higher selectivity and better yield (entry 9). Under these conditions, carbonylation of substituted benzylzinc chlorides was examined.

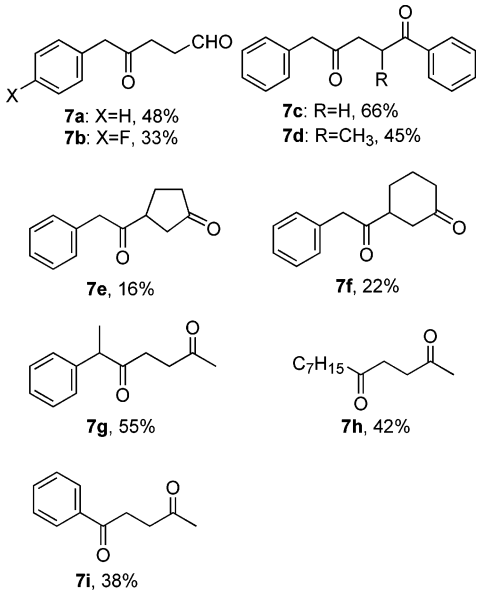


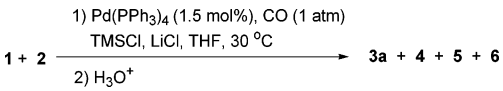
FIGURE 1. Preparation of other 1,4-diketones.

As shown in Table 3, most of the benzylzinc chlorides used were converted into 1,4-diketones **3**. *o*-Substituted benzylzinc chlorides, such as 2-methyl, 2-chloro, 2,6-dichloro, or 2,4,6-trimethylbenzylzinc chloride, afforded 1,4-diketones in better yields.

Other enones, such as acrolein and phenyl vinyl ketone, also produced 1,4-dicarbonyl compounds, **7a**−**d**, in moderate yields (Figure 1). The reactions of cyclic enones, such as cyclopentenone and cyclohexenone, were less effective (**7e**, 16%; **7f**, 22%). More sterically hindered benzylzinc chloride was also carbonylated to give **7g** (55%). Alkylzinc chloride and phenylzinc chloride also produced 1,4-diketones **7h** and **7i** (42% and 38%, respectively). Benzylzinc chloride reacted with neither α,*β*-unsaturated ester nor nitrile under the conditions used.

It was thought that this four-component connecting reaction involved a conjugate addition of benzylzinc chloride, enolate trapping with Me_3SiC1, and carbonyl-

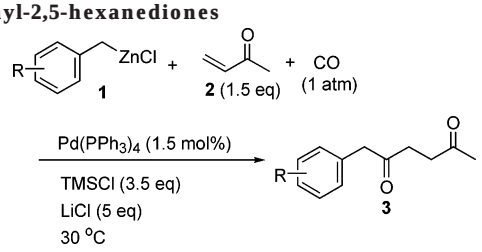
TABLE 2. Preparation of 1-Phenyl-2,5-hexanedione with $Pd(PPh_3)_4$ as a Catalyst



				product yields[a] (%)			
entry	conditions			**3a**	**4**	**5**	**6**
1	**2** (1.0 equiv)	TMSCl (1.0 equiv)	LiCl (1.0 equiv)	40	8	0	1
2	**2** (1.5 equiv)	TMSCl (1.5 equiv)	LiCl (1.5 equiv)	49	8	1	3
3	**2** (1.5 equiv)		LiCl (1.5 equiv)	0	1	3	0
4	**2** (1.5 equiv)	TMSCl (3.5 equiv)	LiCl (1.5 equiv)	52	9	1	4
5	**2** (1.5 equiv)	TMSCl (3.5 equiv)		8	19	0	4
6	**2** (1.5 equiv)	TMSCl (3.5 equiv)	LiCl (3.0 equiv)	55	5	1	7
7	**2** (1.5 equiv)	TMSCl (3.5 equiv)	LiCl (5.0 equiv)	56	2	1	4
8	**2** (1.5 equiv)	TMSCl (3.5 equiv)	NaCl (5.0 equiv)	19	26	2	4
9	**2** (1.5 equiv)	TMSCl (3.5 equiv)[b]	LiCl (5.0 equiv)	65	7	0	1

[a] Product yields were determined by GC analysis. [b] Benzylzinc chloride was added dropwise over a period of 30 min.

TABLE 3. Preparation of Substituted 1-Phenyl-2,5-hexanediones



	R	yield of **3** (%)
a	H	59
b	4-Cl	52
c	4-Br	68
d	4-F	51
e	4-CH_3	52
f	4-OCH_3	19
g	4-$COOCH_3$	80
h	4-CN	40
i	4-Ph	64
j	2-Cl	78
k	2,6-Cl_2	76
l	2-CH_3	82
m	2,4,6-$(CH_3)_3$	60

ation. However, a pathway to a possible intermediate **C** via the formation of β-chloro silyl enol ether (an allyl chloride) is unlikely, because 1,4-addition of TMSCl to methyl vinyl ketone did not occur under the conditions used.[20] Carbonylation via a π-allylpalladium complex generated from an allyl ester followed by alkylation with alkylzinc halide was reported by Tamaru.[21] The formation of η^3-1-siloxyallylnickel(II) chloride in Ni(0)-catalyzed conjugate addition with chlorosilane[18e−i] and the formation of a η^3-1-siloxyallylpalladium(II) complex in Pd(0)-catalyzed conjugate addition with a Lewis acid or Me_3SiOTf[18c,l,m] have been reported. An acylpalladium η^3-allylic complex, corresponding to their acyl derivative, has also been proposed for an intermediate of a 1,4-conjugate addition reaction with acylzirconocene chlorides.[13] In the present work it was not clear whether a similar acylpalladium complex (**F**) was formed. Benzylzinc chloride is stable under CO gas at the ambient temperature. The present carboylation was thus assigned to Pd(0)-catalyzed conjugate addition of benzylzinc chloride to α,β-enones aided by TMSCl, via the formation of a η^3-1-siloxyallylpalladium complex (**B**), followed by carbonylation. This is the first example of transition metal-catalyzed carbonylation of α,β-enones leading to 1,4-diketones.

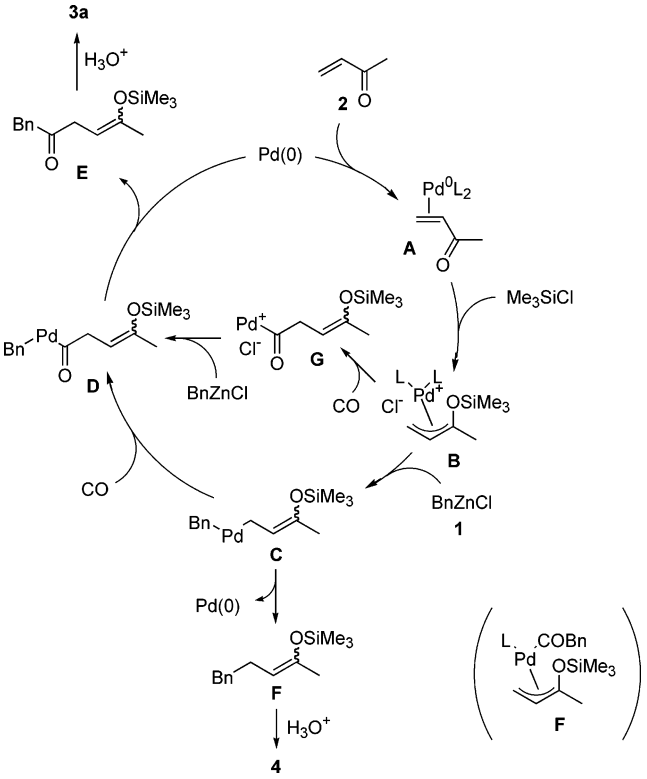


FIGURE 2. Proposed mechanism for the four-component connecting carbonylation.

(16) For conjugate addition of organocopper reagents to enones or related compounds, see the following. With RCu·PBu_3: (a) House, H. O.; Fisher, W. F., Jr. *J. Org. Chem*. **1968**, *33*, 949. (b) Suzuki, M.; Suzuki, T.; Kawagishi, T.; Noyori, R. *Tetrahedron Lett*. **1980**, *21*, 1247. With RCu·BF_3: (c) Yamamoto, Y.; Yamamoto, S.; Yataga, H.; Ishihara, Y.; Maruyama, K. *J. Org. Chem*. **1982**, *47*, 119. With R_2CuLi−TMSCl: (d) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett*. **1985**, *26*, 6015, 6019. (e) Alexakis, A.; Berlian, J.; Besace, Y. *Tetrahedron Lett*. **1986**, *27*, 1047. With RCu·HMPA−TMSCl: (f) Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Tetrahedron Lett*. **1986**, *27*, 4029. With RCu·TMEDA−TMSCl: (g) Johnson, C. R.; Marren, T. J. *Tetrahedron Lett*. **1987**, *28*, 27. With RCu−TMSI: (h) Bergdahl, M.; Eriksson, M.; Nilsson, M.; Olsson, T. *J. Org. Chem*. **1993**, *58*, 7238.

(17) For conjugate addition of RCu(CN)ZnX to enones or related compounds, see: (a) Yeh. M. C. P.; Knochel, P. *Tetrahedron Lett*. **1988**, *29*, 2395. (b) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem*. **1988**, *53*, 2390. (c) Berk, S. C.; Knochel, P.; Yeh. M. C. P. *J. Org. Chem*. **1988**, *53*, 5791. (d) Berk, S. C.; Yeh, M. C. P.; Jeong, N.; Knochel, P. *Organometallics* **1990**, *9*, 3053. (e) Knoess, H. P.; Furlong, M. T.; Rozema, M. J.; Knochel, P. *J. Org. Chem*. **1991**, *56*, 5974. (f) Knochel, P.: Rozema, M. J.; Truker, C. E.; Retherford, C.; Eurlong, M.; AchyuthaRao, S. *Pure Appl. Chem*. **1992**, *64*, 361.

(18) For transition metal-catalyzed conjugate addition of organometallic compounds to α,β-enones or related compounds, see the following. With a Cu(I) catalyst−R_2Zn−TMSCl: (a) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc*. **1984**, *106*, 3368. With Cu(I)−RMgX−TMSCl: (b) Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett*. **1986**, *27*, 4025. With Pd(0)−H_2SiR_2−$ZnCl_2$: (c) Keinan, E.; Greenspoon *J. Am. Chem. Soc*. **1986**, *108*, 7314. With Cu(I)−RZnI−TMSCl: (d) Tamaru, Y.; Tanigawa, H.; Yamamoto, T.; Yoshida, Z.-I. *Angew. Chem., Int. Ed. Engl*. **1989**, *28*, 351. With Ni(0)−RX or RCOX/*hν*-RMe_2SiCl: (e) Johnson, J. R.; Tully, P. S.; Mackenzie, P. B.; Sabat, M. *J. Am. Chem. Soc*. **1991**, *113*, 6172. With Ni(0)−alkenylSnBu$_3$−RMe_2SiCl: (f) Grisso, B. A.; Johnson, J. R.; Mackenzie P. M. *J. Am. Chem. Soc*. **1992**, *114*, 5161. With Ni(0)−alkynylSnBu$_3$−alkyne−TMSCl: (g) Ikeda, S.-i.; Sato, Y. *J. Am. Chem. Soc*. **1994**, *116*, 5975. Ikeda, S.-i.; Kondo, K.; Sato, Y. *J. Org. Chem*. **1996**, *61*, 8248. With Ni(0)−Me_2Zn−alkyne−TMSCl: (h) Ikeda, S.-i.; Yamamoto, H.; Kondo, K.; Sato, Y. *Organometallics* **1995**, *14*, 5015. With Ni(0)−alkynylZn−alkyne−TMSCl: (i) Ikeda, S.-i.; Kondo, K.; Sato, Y. *Chem. Lett*. **1999**, 1227. With Pd(II)−Ar_3Sb: (j) Cho, C. S.; Motofusa, S.-i.; Ohe, K.; Uemura, S. *Bull. Chem. Soc. Jpn*. **1996**, *69*, 2341. With Pd(II)−Ar_4Sn: (k) Ohe, T.; Wakita, T.; Motofusa, S.-i.; Cho, C. S.; Ohe, K.; Uemura S. *Bull. Chem. Soc. Jpn*. **2000**, *73*, 2149. With Pd(0)−R_3Al: (l) Ogoshi, S.; Yoshida, T.; Nishida, T.; Morita, M.; Kurosawa, H. *J. Am. Chem. Soc*. **2001**, *123*, 1944. With Pd(0)−R_3SiSiR_3−Me_3SiOTf: (m) Ogoshi, S.; Tomiyasu, S.; Morita, M.; Kurosawa, H. *J. Am. Chem. Soc*. **2002**, *124*, 11598.

(19) For recent reviews and reports on nickel-, copper-, ruthenium-, rhodium-, or palladium-catalyzed 1,4-conjugate addition reactions with organolithium, boron, magnegium, aluminum, silane, zinc, zirconium, tin, antimony, or mercury reagents, see: (a) Ikeda, S.-i. *Acc. Chem. Res*. **2000**, *33*, 511. (b) Feringa, B. L. *Acc. Chem. Res*. **2000**, *33*, 346. (c) Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033. (d) Krause, N.; Roder, A. H. *Synthesis* **2001**, 171. (e) Hayashi, T.; Yamasaki, K. *Chem. Rev*. **2003**, *103*, 2829.

(20) For 1,4-addition of $ISiMe_3$ to α,β-unsaturated systems, see: Miller, R. D.; McKean, D. R. *Tetrahedron Lett*. **1979**, 2305. HCl was added to methyl vinyl ketone to give 4-chloro-2-butanone, which remained unchanged under the conditions.

(21) Tamaru, Y.; Yasui, K.; Takanabe, H.; Tanaka, S.; Fugami, K. *Angew. Chem., Int. Ed. Engl*. **1992**, *31*, 5. Yasui, K.; Fugami, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem*. **1995**, *60*, 1365.

Insertion of a CO molecule into this palladium η^1-allylic complex **C** followed by reductive elimination of Pd(0) from the resultant acylpalladium complex **D** gave silyl enol ethers **E**, nonstereoselectively, which on acidic workup afforded diketone **3a**. Silyl enol ether **E**[22] was obtained in an 8:7 *E*/*Z* ratio from methyl vinyl ketone when the workup with diluted HC1 solution was omitted. Ketone **4** is probably formed by elimination of Pd(0). In fact, execution of this reaction in the absence of CO gas under nitrogen produced **4** in 78% yield.

Interestingly, *o*-substituted benzylzinc chlorides **2j**−**m** underwent carbonylation smoothly to provide the corresponding diketones (**3j**−**m**) in higher yields than those obtained from *p*-substituted benzylzinc chlorides, although it is expected that transmetalation of such sterically hindered reagents (**B** to **C**) proceeds more slowly. This suggests the existence of an alternative pathway, such as **B** → **G** → **D**, in which a direct carbonylation on **B** precedes the transmetalation.

Byproducts 1,2-diphenylethane (**5**) and 1,3-diphenylacetone (**6**) were formed probably from the unchanged benzylic chlorides by their Pd(0)-catalyzed dimerization or carbonylative dimerization in small amounts (Table 2).

At present, we do not have evidence for the role of lithium chloride. The formation of a more nucleophilic Pd(0) species [$L_2Pd^0Cl^-$] in Heck and cross-coupling reactions has been proposed by Amatore and Jutand,[23,24] who have also reported that the oxidative addition is faster in the presence of a lithium cation due to the generation of a more "naked" and thus more reactive Pd(0) complex [$L_2Pd^0\cdots Cl^-\cdots Li^+$]. The oxidative addition of such a Pd(0) species into enone **2** must proceed more smoothly to afford intermediate **B** efficiently. Thus, we assume the in situ generation of such a reactive palladium catalyst by addition of LiCl, although alternative explanations for the effect of LiCl, such as inhibition of β-hydrogen elimination,[25] protection from the cleavage of THF molecules with halosilane,[26] and enhancement of solubility of a metal complex[27] have been proposed.

By conventional methods based on Paal or Paal−Knorr-type synthesis,[6,28] the obtained 1,4-dicarbonyl compounds, **3a**, **7c**, and **7i**, were smoothly converted into furan **8a** or **8b** with P_2O_5, pyrrole **9a**, **9b**, or **9c** with $AcONH_4$ or benzylamine, or thiophene **10** with P_2S_5 in good yield as shown in Figure 3. Cyclopentenones **11a** and **11b** were also prepared from diketones **3a** and **3c** by treatment with EtONa in EtOH in 94% or 61% yields, respectively.

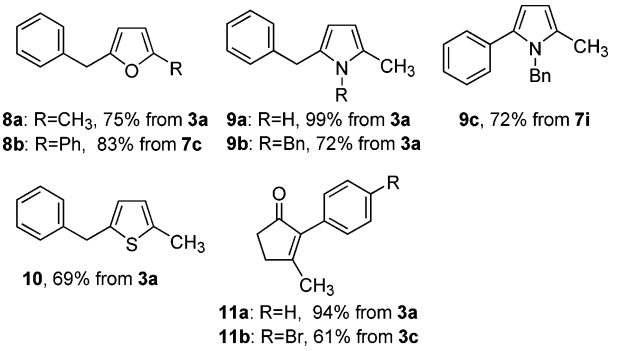


FIGURE 3. Preparation of five-membered heterocyclic compounds from the obtained 1,4-diketones.

Thus, Pd(0)-catalyzed carbonylation of benzylzinc chlorides with methylvinyl ketone or the analogous α,β-unsaturated ketones in the presence of TMSCl and LiCl under CO (1 atm) has been demonstrated to undergo 1,4-acylation to afford a variety of 1-phenyl-2,5-hexadiones or related dicarbonyl compounds. Some of them were successively converted into cyclopentenones or five-membered heterocyclic compounds such as pyrrole, furan, or thiophene.

Experimental Section

Anhydrous tetrahydrofuran was purchased from Kanto Chemical Co. Inc. Zinc metal was purchased from Aldrich (dust, <10 μm) and activated by washing with dilute hydrochloric acid. Column chromatography was conducted with use of Cica-reagent silica gel 60 (100−210 mm, spherical, Kanto Chemical Co. Inc.). NMR spectra were measured in $CDCl_3$ (99.8 atom % D, containing 0.03% v/v TMS, Aldrich) on a 270- or 400-MHz spectrometer. Mass spectra were recorded by EI ionization at 70 eV.

Typical Procedure for the Preparation of Benzylzinc Halide. A flask containing zinc dust (10.0 g, 150 mmol, activated by washing with a dilute HCl solution[29]) was purged with Ar gas. Into this was added THF (50 mL) and TMSCl (0.5 mL). After the mixture was stirred for 15 min, benzyl chloride (11.8 mL, 100 mmol) was added dropwise. The mixture was warmed at 40 °C for 4 h, and then cooled to room temperature. The resulting clear benzylzinc chloride solution (55 mL, 1.82 M) could be stored under Ar gas for a few months.

Typical Procedure for the Preparation of 1,4-Diketones 3: 1-Phenylhexane-2,5-dione (3a) (Table 3). To a stirred mixture of LiCl (471 mg, 11.1 mmol) and $Pd(Ph_3P)_4$ (38 mg, 0.03 mmol) in THF (3 mL) was added TMSCl (0.98 mL, 7.7 mmol) and methyl vinyl ketone (0.27 mL, 3.3 mmol) under CO gas (1 atm). After 10 min, benzylzinc chloride solution (1.82 M in THF, 1.20 mL, 2.2 mmol) was added dropwise into the mixture over a period of 30 min with vigorous stirring at 30 °C. After 5 min, the reaction was

(22) A pale yellow oil; bp 120−125 °C/0.5 mmHg (5:6 *E*/*Z* mixture). *E*-isomer: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.15 (s, 9H), 1.81 (s, 3H), 3.13 (dd, J = 6.9, 1.0 Hz, 2H), 3.71 (s, 2H), 4.61 (td, J = 6.9, 1.0 Hz, 1H), 7.37−7.13 (m, 5H). *Z*-isomer: ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.19 (s, 9H), 1.67 (s, 3H), 3.07 (d, J = 7.6 Hz, 2H), 3.72 (s, 2H), 4.76 (td, J = 7.6, 1.0 Hz, 1H), 7.37−7.13 (m, 5H). In the NOESY of these enol silyl ethers, significant NOE effect between 6-Me (δ 1.81) and 3-H_2 (δ 3.71) of the *E*-isomer and 4-H (δ 4.76) and 6-Me (δ 1.67) of the *Z*-isomer were observed.

(23) (a) For a review, see: Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314.

(24) (a) Amatore, C.; Azzabi, M.; Jutand, A. *J. Organomet. Chem.* **1989**, *363*, C41. (b) Amatore, C.; Azzabi, M.; Jutand, A. *J. Am. Chem. Soc.* **1991**, *113*, 8375. Cf.: (c) Negishi, E.-i.; Takahashi, T.; Akiyoshi, K. *J. Chem. Soc., Chem. Commun.* **1986**, *1338*. Cf.: (d) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033.

(25) (a) Wang, Z.; Zhang, Z.; Lu, X.*Organometallic*s **2000**, *19*, 775. (b) Zhang, Z.; Lu, X.; Zhang, Q.; Han, X. *Organometallic*s **2001**, *20*, 3724. (c) Liu, G.; Lu, X. *Tetrahedron Lett.* **2002**, *43*, 6791.

(26) Bergdahl, M.; Eriksson, M.; Nilsson, M.; Olsson T. *J. Org. Chem.* **1993**, *58*, 7244.

(27) Alexakis, A.; Berlan, J.; Besace, Y. *Tetrahedron Lett.* **1986**, *27*, 1047.

(28) For furans, thiophens, and pyrroles, see: (a) Sir Robinson, R.; Todd, W. M. *J. Chem. Soc.* **1939**, *39*, 1743. For furans, see: (b) Nowlin, G. *J. Am. Chem. Soc.* **1950**, *72*, 5755 and ref 6a. For thiophens, see: (c) Wynberg, H.; Metselaar, J. *Synth. Commun.* **1984**, *14*, 1. For pyrroles, see: (d) Stetter, H.; Jonas, F. *Chem Ber.* **1981**, *114*, 564. (e) Stetter, H.; Mohrmann, K. H.; Schlenker, W. K. H. *Synthesis* **1981**, 129. (f) Lui, H.; Sammes, M. P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 457. (g) Boga, C.; Manescalch, F.; Savoia, D. *Tetrahedron Lett.* **1994**, *50*, 4709. (h) Hori, M.; Mori, M. *J. Org. Chem.* **1995**, *60*, 1480.

(29) Shriner, R. L.; Newmann, F. W. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 73.

quenched with 2 N HCl solution (2 mL), diluted with water (10 mL), and extracted with Et_2O (20 mL × 2). The combined organic layers were washed with water (10 mL) and brine (10 mL) and dried over $MgSO_4$. The extract was concentrated, and the residue was subjected to column chromatography on silica gel (3:1 hexane/EtOAc) to afford dione **3a** (247 mg, 59%) as a colorless oil, bp 145 °C/1.0 mmHg [lit.[30] bp 105−107 °C/0.01 mmHg]; IR (neat) 1713 cm^{-1}; ^1H NMR (400 MHz) δ 2.16 (s, 3H), 2.73−2.66 (m, 4H), 3.75 (d, J = 4.6 Hz, 2H), 7.37−7.20 (m, 5H); ^{13}C NMR (100 MHz) δ 29.9 (q), 35.5 (t), 37.0 (t), 50.0 (t), 127.0 (d), 128.6 (d), 129.4 (d), 134.1 (s), 207.0 (s), 207.1 (s); EI-MS m/z (rel intensity) 190 (M^+, 8), 99 (100), 91 (31), 71 (12). These spectral data were essentially identical with those reported previously.[30,31]

1-(4-Chlorophenyl)hexane-2,5-dione (3b): Column chromatography with 5:1 hexane/EtOAc; colorless crystals (52%); mp 60.5−62.3 °C (Et_2O−hexane); IR (neat) 1705, 1492 cm^{-1}; ^1H NMR (400 MHz) δ 2.17 (s, 3H), 2.71 (s, 4H), 3.74 (s, 2H), 7.13 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz) δ 29.8 (q), 35.6 (t), 37.0 (t), 49.1 (t), 128.7 (d), 130.8 (d), 132.5 (s), 132.9 (s), 206.3 (s), 207.5 (s); EI-MS m/z (rel intensity) 224 (M^+, 12), 125 (23), 99 (100), 71 (13). Anal. Calcd for $C_{12}H_{13}ClO_2$: C, 64.15; H, 5.83; Cl, 15.78. Found: C, 64.25; H, 5.98; Cl, 15.83.

1-(4-Bromophenyl)hexane-2,5-dione (3c): 3:1 hexane/EtOAc; colorless crystals (68%); mp 75.0−75.6 °C (Et_2O−hexane); IR (neat) 1703, 1488 cm^{-1}; ^1H NMR (400 MHz) δ 2.17 (s, 3H), 2.71 (s, 4H), 3.72 (s, 2H), 7.09 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H); ^{13}C NMR (100 MHz) δ 29.9 (q), 35.6 (t), 37.0 (t), 49.2 (t), 121.0 (s), 131.2 (d), 131.7 (d), 133.0 (s), 206.2 (s), 207.0 (s); EI-MS m/z (rel intensity) 268 (M^+, 7), 169 (12), 99 (100), 71 (14). Anal. Calcd for $C_{12}H_{13}BrO_2$: C, 53.55; H, 4.87; Br, 29.69. Found: C, 53.74; H, 4.90; Br, 29.47.

1-(4-Fluorophenyl)hexane-2,5-dione (3d): 3:1 hexane/EtOAc; a colorless oil (51%); bp 119 °C/0.3 mmHg; IR (neat) 1714, 1603, 1511 cm^{-1}; ^1H NMR (400 MHz) δ 2.19 (s, 3H), 2.72 (s, 4H), 3.74 (s, 2H), 7.01 (m, 2H), 7.16 (m, 2H); ^{13}C NMR (100 MHz) δ 29.9 (q), 35.5 (t), 37.0 (t), 48.9 (t), 115.4 (d), 115.6 (d), 129.8 (s), 130.9 (d), 131.0 (d), 163.1 (s), 206.7 (s), 207.1 (s); EI-MS m/z (rel intensity) 208 (M^+, 13), 109 (39), 99 (100), 71 (14). Anal. Calcd for $C_{12}H_{13}FO_2$: C, 69.22; H, 6.29; F, 9.12. Found: C, 69.21; H, 6.34; F, 9.02.

1-(4-Tolyl)hexane-2,5-dione (3e): 5:1 hexane/EtOAc; a colorless oil (52%); bp 180 °C/30 mmHg; IR (neat) 1711, 1515 cm^{-1}; ^1H NMR (270 MHz) δ 2.16 (s, 3H), 2.32 (s, 3H), 2.68 (m, 4H), 3.70 (s, 2H), 7.09 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz) δ 21.1 (q), 29.9 (q), 35.4 (t), 37.0 (t), 49.7 (t), 129.3 (d), 129.4 (d), 131.1 (s), 136.7 (s), 207.19 (s), 207.23 (s); EI-MS m/z (rel intensity) 204 (M^+, 28), 105 (41), 99 (100), 71 (12). These spectral data were essentially identical with those reported by Kametani.[4b]

1-(4-Methoxyphenyl)hexane-2,5-dione (3f): 2:1 hexane/EtOAc; a colorless oil (19%); bp 155 °C/0.2 mmHg [lit.[30] bp 120−123 °C/0.01 mmHg]; IR (neat) 1711, 1611, 1584, 1513 cm^{-1}; ^1H NMR (270 MHz) δ 2.16 (s, 3H), 2.69 (m, 4H), 3.68 (s, 2H), 3.79 (s, 3H), 6.86 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H); ^{13}C NMR (68 MHz) δ 29.9 (q), 35.3 (t), 37.0 (t), 49.1 (q), 55.2 (t), 113.9 (d), 128.6 (s), 130.4 (d), 158.6 (s), 207.2 (s), 207.4 (s).

1-[(4-Methoxycarbonyl)phenyl]hexane-2,5-dione (3g): 2:1 hexane/EtOAc; a colorless oil (80%); bp 206 °C/1.5 mmHg; IR (neat) 1718, 1714, 1613, 1576, 1510 cm^{-1}; ^1H NMR (270 MHz) δ 2.17 (s, 3H), 2.71 (m, 4H), 3.82 (s, 2H), 3.90 (s, 3H), 7.28 (d, J = 8.3 Hz, 2H), 8.00 (d, J = 8.3 Hz, 2H); ^{13}C NMR (68 MHz) δ 29.8 (q), 35.7 (t), 37.0 (t), 49.7 (t), 52.0 (q), 128.8 (s), 129.5 (d), 129.8 (d), 139.2 (s), 166.8 (s), 205.9 (s), 206.9 (s); EI-MS m/z (rel intensity) 248 (M^+, 4), 217 (11), 150 (22), 118 (8), 99 (100), 71 (13). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.53; H, 6.47.

1-(4-Cyanophenyl)hexane-2,5-dione (3h): recrystallized from Et_2O−hexane; colorless crystals (40%); mp 107.9−110.4 °C (Et_2O−hexane); IR (neat) 2226, 1702, 1608, 1505 cm^{-1}; ^1H NMR (400 MHz) δ 2.18 (s, 3H), 2.74 (s, 4H), 3.86 (s, 2H), 7.31 (d, J = 7.8 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz) δ 29.8 (q), 36.0 (t), 37.1 (t), 49.6 (t), 100.5 (s), 118.7 (s), 130.4 (d), 132.3 (d), 139.4 (s), 205.3 (s); EI-MS m/z (rel intensity) 215 (M^+, 2), 116 (21), 99 (100), 71 (13). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.21; H, 6.14; N, 6.34.

1-(Biphenyl-4-yl)hexane-2,5-dione (3i): 4:1 hexane/EtOAc; colorless crystals (64%); mp 73.9−76.2 °C (Et_2O−hexane); IR (neat) 1704, 1490 cm^{-1}; ^1H NMR (400 MHz) δ 2.18 (s, 3H), 2.73 (m, 4H), 3.78 (s, 2H), 7.27 (m, 2H), 7.34 (m, 1H), 7.43 (m, 2H), 7.57 (m, 4H); ^{13}C NMR (100 MHz) δ 29.9 (q), 35.6 (t), 37.0 (t), 49.6 (t), 127.0 (d), 127.3 (s), 127.4 (d), 128.7 (d), 129.9 (d), 133.1 (s), 139.0 (s), 140.7 (s), 206.9 (s), 207.2 (s); EI-MS m/z (rel intensity) 266 (M^+, 31), 167 (52), 99 (100), 71 (7). Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.27; H, 6.94.

1-(2-Chlorophenyl)hexane-2,5-dione (3j): 5:1 hexane/EtOAc; a colorless oil (78%); bp 131 °C/0.2 mmHg [lit.[30] bp 140−144 °C/0.01 mmHg]; IR (neat) 1712, 1574, 1475 cm^{-1}; ^1H NMR (270 MHz) δ 2.17 (s, 3H), 2.78−2.68 (m, 4H), 3.89 (s, 2H), 7.39−7.19 (m, 4H); ^{13}C NMR (68 MHz) δ 29.8 (q), 35.8 (t), 36.8 (t), 47.4 (t), 126.9 (d), 128.5 (d), 129.3 (d), 131.7 (d), 132.5 (s), 134.2 (s), 205.5 (s), 207.0 (s); EI-MS m/z (rel intensity) 224 (M^+, 2), 125 (11), 99 (100), 71 (12). Anal. Calcd for $C_{12}H_{13}ClO_2$: C, 64.15; H, 5.83; Cl, 15.78. Found: C, 64.13; H, 5.92; Cl, 15.83.

1-(2,6-Dichlorophenyl)hexane-2,5-dione (3k): 5:1 hexane/EtOAc; colorless crystals (76%); mp 58.7−59.4 °C (Et_2O−hexane); IR (neat) 1733, 1720, 1583, 1562 cm^{-1}; ^1H NMR (270 MHz) δ 2.16 (s, 3H), 2.83−2.71 (m, 4H), 4.13 (s, 2H), 7.13 (dd, J = 8.6, 7.3 Hz, 1H), 7.29 (d, J = 7.3 Hz, 2H); ^{13}C NMR (68 MHz) δ 29.6 (q), 35.6 (t), 36.6 (t), 44.8 (t), 127.7 (d), 128.6 (d), 131.4 (s), 135.7 (s), 203.8 (s), 206.6 (s); EI-MS m/z (rel intensity) 258 (M^+, 0.1), 159 (7), 99 (100), 71 (13). Anal. Calcd for $C_{12}H_{12}Cl_2O_2$: C, 55.62; H, 4.67; Cl, 27.36; O, 12.35. Found: C, 55.75; H, 4.81; Cl, 27.36.

1-(2-Tolyl)hexane-2,5-dione (3l): 5:1 hexane/EtOAc; a colorless oil (82%); bp 149 °C/1.3 mmHg; IR (neat) 1715, 1493 cm^{-1}; ^1H NMR (400 MHz) δ 2.16 (s, 3H), 2.24 (s, 3H), 2.68 (s, 4H), 3.76 (s, 2H), 7.20−7.13 (m, 4H); ^{13}C NMR (100 MHz) δ 19.6 (q), 29.8 (q), 35.4 (t), 36.9 (t), 48.1 (t), 126.2 (d), 127.3 (d), 130.35 (d), 130.37 (d), 133.0 (s), 136.9 (s), 206.9 (s), 207.1 (s); EI-MS m/z (rel intensity) 204 (M^+, 9), 105 (27), 99 (100), 71 (12). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.44; H, 8.01.

1-(2,4,6-Trimethylphenyl)hexane-2,5-dione (3m): 3:1 hexane/EtOAc; a colorless oil (60%); bp 129 °C/0.2 mmHg, mp 29−31 °C (Et_2O−hexane) [lit.[32] mp 32 °C]; IR (neat) 1711, 1614, 1486 cm^{-1}; ^1H NMR (270 MHz) δ 2.16 (s, 3H), 2.21 (s, 6H), 2.25 (s, 3H), 2.66 (m, 4H), 3.77 (s, 2H), 6.86 (s, 2H); ^{13}C NMR (68 MHz) δ 20.2 (t), 20.8 (t), 29.8 (t), 35.3 (t), 36.9 (t), 43.9 (t), 128.8 (d), 136.3(s), 136.7 (s), 207.06 (s), 207.09 (s); EI-MS m/z (rel intensity) 232 (M^+, 14), 133 (88), 99 (100), 71 (7).

4-Oxo-5-phenylpentanal (7a): 4:1 hexane/EtOAc; a colorless oil (48%); bp 108 °C/0.4 mmHg; IR (neat) 2730, 1721, 1714, 1604, 1497 cm^{-1}; ^1H NMR (270 MHz) δ 2.74 (m, 4H), 3.75 (s, 2H), 7.36−7.16 (m, 5H), 9.77 (s, 1H); ^{13}C NMR (68 MHz) δ 34.0 (t), 37.5 (t), 50.0 (t), 127.1 (d), 128.7 (d), 129.4 (d), 134.1 (s), 200.4 (d), 206.3 (s); EI-MS m/z (rel intensity) 176 (M^+, 24), 91 (56), 85 (100), 57 (7). Anal. Calcd for $C_{14}H_{16}O_2$: C, 74.98; H, 6.86. Found: C, 74.88; H, 6.66.

4-Oxo-5-(4-fluorophenyl)pentanal (7b): 3:1 hexane/EtOAc; a colorless oil (33%); bp 117 °C/0.4 mmHg; IR (neat) 2734, 1718, 1604, 1510 cm^{-1}; ^1H NMR (400 MHz) δ 2.76 (s, 4H), 3.74 (s, 2H), 7.02 (m, 2H), 7.16 (m, 2H), 9.77 (s, 1H); ^{13}C

(30) Stetter, H.; Lorenz, G. *Chem. Ber.* **1985**, *118*, 1115.
(31) Pecunioso, A.; Menicagli R. *J. Org. Chem.* **1988**, *53*, 2614.
(32) Eberhardt, U.; Deppisch, B.; Musso, H. *Chem. Ber.* **1983**, *116*, 119.

NMR (100 MHz) δ 34.0 (t), 37.5 (t), 48.9 (t), 115.5 (d), 115.7 (d), 129.6 (s), 130.9 (d), 131.0 (d), 163.2 (s), 200.2 (d), 206.0 (s). Anal. Calcd for $C_{11}H_{11}FO_2$: C, 68.03; H, 5.71; F, 9.78. Found: C, 67.94; H, 5.81; F, 9.70.

1,5-Diphenylpentane-1,4-dione (7c): 3:1 hexane/EtOAc; a colorless oil (66%); bp 149 °C/0.2 mmHg (lit.[30] mp 59−60 °C); IR (neat) 1709, 1686, 1598, 1583, 1498 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.89 (t, J = 6.1 Hz, 2H), 3.24 (t, J = 6.1 Hz, 2H), 3.82 (s, 2H), 7.35−7.23 (m, 5H), 7.44 (t, J = 7.6 Hz, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.95 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz) δ 32.5 (t), 35.6 (t), 50.2 (t), 127.0 (d), 128.0 (d), 128.5 (d), 128.7 (d), 129.5 (d), 133.1 (d), 134.2 (s), 136.5 (s), 198.4 (s), 207.0 (s); EI-MS m/z (rel intensity) 252 (M$^+$, 1.4), 161 (100), 133 (22), 105 (69), 91 (27), 77 (43).

1,5-Diphenyl-2-methylpentane-1,4-dione (7d): 4:1 hexane/EtOAc; a colorless oil (45%); bp 173 °C/0.3 mmHg; IR (neat) 1715, 1686, 1598, 1580, 1498 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.12 (d, J = 7.3 Hz, 3H), 2.56 (dd, J = 17.8, 4.8 Hz, 1H), 3.17 (dd, J = 17.8, 8.6 Hz, 1H), 3.90 (s, 2H), 3.94 (m, 1H), 7.35−7.18 (m, 5H), 7.56−7.41 (m, 3H), 7.95 (d, J = 6.9 Hz, 2H); ^{13}C NMR (68 MHz) δ 17.6 (q), 36.1 (t), 45.2 (d), 50.0 (t), 126.9 (d), 128.3 (d), 128.5 (d), 128.6 (d), 129.3 (d), 132.8 (d), 133.9 (s), 135.8 (s), 203.1 (s), 206.7 (s); EI-MS m/z (rel intensity) 266 (M$^+$, 1.6), 175 (100), 105 (98), 91 (19), 77 (21). Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.07; H, 6.91.

3-(Phenylacetyl)cyclopentanone (7e): 3:1 hexane/EtOAc; a colorless oil (16%); bp 106 °C/0.2 mmHg; IR (neat) 1743, 1708, 1603, 1497 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.05−1.96 (m, 1H), 2.36−2.14 (m, 4H), 2.47 (dd, J = 18.5, 8.8 Hz, 1H), 3.34 (m, 1H), 3.81 (s, 2H), 7.21 (d, J = 7.6 Hz, 2H), 7.37−7.26 (m, 3H); ^{13}C NMR (100 MHz) δ 26.1 (t), 37.5 (t), 40.4 (t), 46.8 (d), 49.1 (t), 127.3 (d), 128.9 (d), 129.4 (d), 133.4 (s), 208.1 (s), 216.5 (s); EI-MS m/z (rel intensity) 202 (M$^+$, 29), 111 (32), 91 (88), 83 (69), 55 (100). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.93; H, 7.22.

3-(Phenylacetyl)cyclohexanone (7f): 4:1 hexane/EtOAc; a colorless oil (22%); bp 168 °C/1.8 mmHg; IR (neat) 1709, 1497 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.72−1.67 (m, 2H), 2.08−2.02 (m, 2H), 2.37−2.29 (m, 3H), 2.51 (dd, J = 14.4, 11.2 Hz, 1H), 2.99 (m, 1H), 3.76 (d, J = 2.2 Hz, 2H), 7.18 (d, J = 7.3 Hz, 2H), 7.35−7.25 (m, 3H); ^{13}C NMR (100 MHz) δ 24.7 (t), 27.3 (t), 40.8 (t), 42.5 (t), 48.3 (d), 49.2 (t), 127.2 (d), 128.7 (d), 129.3 (d), 133.4 (s), 207.9 (s), 209.8 (s); EI-MS m/z (rel intensity) 216 (M$^+$, 28), 125 (20), 97 (100), 91 (60), 69 (51). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.94; H, 7.46.

6-Phenylheptane-2,5-dione (7g): 3:1 hexane/EtOAc; a colorless oil (55%); bp 98 °C/0.3 mmHg; IR (neat) 1717, 1712, 1600, 1561, 1495 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.40 (d, J = 6.9 Hz, 3H), 2.15 (s, 3H), 2.75−2.51 (m, 4H), 3.82 (q, J = 6.93 Hz, 1H), 7.36−7.20 (m, 5H); ^{13}C NMR (68 MHz) δ 17.3 (q), 29.9 (q), 34.6 (t), 37.1 (t), 52.9 (d), 127.1 (d), 127.8 (d), 128.8 (d), 140.5 (s), 207.2 (s), 209.5 (s); EI-MS m/z (rel intensity) 204 (M$^+$, 2), 105 (24), 99 (100), 71 (13). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.32; H, 7.87.

***n*-Dodecane-2,5-dione (7h):** 5:1 hexane/EtOAc; light brown crystals (42%); mp 35.9−38.3 °C (Et_2O−hexane) [lit.[33] mp 40−41 °C]; IR (neat) 1704, 1699 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.87 (t, J = 6.9 Hz, 3H), 1.27 (br s, 8H), 1.57 (br quint, J = 7.3 Hz, 2H), 2.19 (s, 3H), 2.45 (t, J = 7.3 Hz, 2H), 2.70−2.65 (m, 4H); ^{13}C NMR (68 MHz) δ 14.0 (q), 22.5 (t), 23.8 (t), 29.00 (t), 29.07 (t), 29.9 (q), 31.6 (t), 36.0 (t), 36.8 (t), 42.8 (t), 207.2 (s), 209.6 (s); EI-MS m/z (rel intensity) 198 (M$^+$, 6), 155 (6), 127 (25), 114 (100), 99 (56), 71 (83), 43 (46).

1-Phenylpentane-1,4-dione (7i): 4:1 hexane/EtOAc; a colorless oil (38%); bp 109 °C/0.2 mmHg [lit.[34] 100−103 °C/2 mmHg]; IR (neat) 1718, 1686, 1598 cm^{-1}; ^{1}H NMR (270 MHz) δ 2.26 (s, 3H), 2.88 (t, 2H), 3.28 (t, J = 6.6 Hz, 2H), 7.60−7.20 (m, 3H), 7.98 (d, J = 7.3 Hz, 2H); ^{13}C NMR (68 MHz) δ 30.0 (q), 32.7 (t), 37.0 (t), 128.0 (d), 128.5 (d), 133.1 (s), 207.3 (s); EI-MS m/z (rel intensity) 176 (M$^+$, 8), 161 (23), 133 (12), 105 (100), 77 (44), 43 (18).

2-Benzyl-5-methylfuran (8a). To a solution of 1-phenylhexane-2,5-dione (**3a**, 38 mg, 0.2 mmol) in toluene (3 mL) was added P_2O_5 (57 mg, 0.4 mmol), and the mixture was refluxed with stirring for 2 h. The reaction mixture was poured into water (10 mL), extracted with CH_2Cl_2 (2 × 10 mL), and dried (Na_2SO_4). The solvent was removed in vacuo, and the residue was subjected to column chromatography on silica gel eluted with 20:1 hexane/EtOAc to afford **8a** as a pale yellow oil (26.3 mg, 76%). IR (neat) 1698, 1604, 1568, 1495 cm^{-1}; ^{1}H NMR (270 MHz) δ 2.24 (s, 3H), 3.91 (s, 2H), 5.85 (s, 2H), 7.30−7.21 (m, 5H); ^{13}C NMR (68 MHz) δ 152.7 (s), 138.5 (s), 128.7 (d), 128.4 (d), 126.4 (d), 106.9 (d), 106.0 (d), 34.6 (t), 13.6 (q). These spectral data were essentially identical with those reported by Wu.[35]

2-Benzyl-5-phenylfuran (8b). To a solution of **7c** (50.4 mg, 0.2 mmol) in toluene (3 mL) was added P_2O_5 (57 mg, 0.4 mmol) and the mixture was stirred with reflux for 15 h. The reaction mixture was poured into water (10 mL), extracted with CH_2Cl_2 (2 × 10 mL), and dried (Na_2SO_4). The solvent was evaporated to give an oily residue, which was subjected to column chromatography on silica gel eluted with 20:1 hexane−EtOAc to afford **8b** (31.2 mg, 83%) as a colorless oil. IR (neat) 1685, 1596, 1544, 1489 cm^{-1}; ^{1}H NMR (270 MHz) δ 4.04 (s, 2H), 6.06 (d, J = 3.3 Hz, 1H), 6.55 (d, J = 3.3 Hz, 1H), 7.40−7.18 (m, 8H), 7.62 (d, J = 7.3 Hz, 2H); ^{13}C NMR (68 MHz) δ 34.6 (t), 105.7 (d), 108.4 (d), 123.4 (d), 126.5(d), 126.9 (d), 128.47 (d), 128.54 (d), 128.7 (d), 131.0 (s), 138.0 (s), 152.8 (s), 154.3 (s). EI-MS m/z (rel intensity) 234 (M$^+$, 100), 157 (40), 105 (30), 91 (21), 77 (24); HRMS calcd for $C_{17}H_{14}O$ 234.1045, found 234.1038.

2-Benzyl-5-methylpyrrole (9a). A mixture of **3a** (76 mg, 0.4 mmol) and NH_4OAc (493 mg, 6.4 mmol) in AcOH (5 mL) was heated at 110 °C for 1 h and, after cooling to room temperature, was poured onto water (10 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with 2 N NaOH solution (10 mL) and water (10 mL) and then dried (Na_2SO_4). The solvent was evaporated to leave an oily residue, which was subjected to column chromatography on silica gel eluted with 10:1 hexane−EtOAc to afford **9a** (75.4 mg, 99%) as a colorless oil. IR (neat) 3458, 1590, 1495 cm^{-1}; ^{1}H NMR (270 MHz) δ 2.19 (s, 3H), 3.91 (s, 2H), 5.78 (s, 1H), 5.84 (s, 1H), 7.33−7.10 (m, 5H), 7.49 (br s, 1H); ^{13}C NMR (68 MHz) δ 13.0 (q), 34.1 (t), 105.7 (d), 106.4 (d), 126.2 (d), 128.1 (s), 128.5 (d), 128.6 (d), 129.2 (s), 139.8 (s). These spectral data were essentially identical with those reported previously.[36]

1,2-Dibenzyl-5-methylpyrrole (9b). A solution of **3a** (190 mg, 1.0 mmol) and benzylamine (107 mg, 1.0 mmol) in toluene (10 mL) was refluxed for 20 h and concentrated to afford an oily residue, which was subjected to column chromatography on silica gel eluted with 5:1 hexane−EtOAc to afford **9b** (238 mg, 91%) as a colorless oil. Bp 113 °C/0.3 mmHg; IR (neat) 1604, 1513, 1495 cm^{-1}; ^{1}H NMR (270 MHz) δ 2.13 (s, 3H), 3.80 (s, 2H), 4.91 (s, 2H), 5.87 (dd, J = 14.2, 3.3 Hz, 2H), 6.83 (d, J = 7.3 Hz, 2H), 7.27−7.09 (m, 8H); ^{13}C NMR (68 MHz) δ 12.4 (q), 33.2 (t), 46.7 (t), 105.6 (d), 107.0 (d), 125.6 (d), 126.1(d), 126.9 (d), 128.3 (d), 128.5 (d), 128.6 (d), 128.7 (s), 130.8(s), 138.5 (s), 139.6 (s), 261 (M$^+$, 42), 184 (19), 170 (18), 91 (100), 71 (7). Anal. Calcd for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found: C, 87.06; H, 7.50; N, 5.10.

1-Benzyl-5-methyl-2-phenylpyrrole (9c). A solution of **7i** (200 mg, 1.14 mmol) and benzylamine (128 mg, 1.2 mmol) in toluene (10 mL) was refluxed for 20 h and concentrated to leave an oily residue, which was subjected to column chromatography on silica gel eluted with 10:1 hexane−EtOAc to afford **9c** (202 mg, 72%) as a colorless oil. IR (neat) 1603, 1514, 1496 cm^{-1}; ^{1}H NMR (270 MHz) δ 2.13 (s, 3H), 5.12 (s, 2H),

(33) Stetter, H.; Kuhlmann, H. *Chem. Ber.* **1976**, *109*, 3426.
(34) Lu, X.; Ji, J.; Ma, D.; Shen, W. *J. Org. Chem.* **1991**, *56*, 5774.
(35) Wu, H. J.; Lin, C. C. *J. Org. Chem.* **1995**, *60*, 7558.
(36) Nagafuji, P.; Cushman, M. *J. Org. Chem.* **1996**, *61*, 4999.

6.04 (d, $J = 3.3$ Hz, 1H), 6.23 (d, $J = 3.3$ Hz, 1H), 6.92 (d, $J = 6.9$ Hz, 2H), 7.32−7.18 (m, 5H); ^{13}C NMR (68 MHz) δ 12.6 (q), 47.6 (t), 107.1 (d), 107.9 (d), 125.6 (d), 126.6(d), 126.9 (d), 128.3 (d), 128.6 (d), 128.7 (d), 130.4 (s), 133.7 (s), 134.6 (s), 138.9 (s); EI-MS *m*/*z* (rel intensity) 247 (M^+, 85), 170 (2), 156 (81), 91 (100), 77 (5). HRMS calcd for $C_{18}H_{17}N$ 247.1361, found 247.1362.

2-Benzyl-5-methylthiophen (10). To a solution of **3a** (76 mg, 0.4 mmol) in toluene (4 mL) was added P_2S_5 (89 mg, 0.4 mmol), and the mixture was refluxed with stirring for 12 h. The reaction mixture was purified by column chromatography on silica gel (hexane) to afford **10** (52 mg, 69%) (lit.[37] bp 74−76 °C, mp 5 °C). IR (neat) 1493 cm^{-1}; ^{1}H NMR (270 MHz) δ 2.41 (s, 3H), 4.07 (s, 2H), 6.56 (d, $J = 2.3$ Hz, 2H), 7.40−7.15 (m, 5H); ^{13}C NMR (68 MHz) δ 15.3 (q), 36.2 (t), 106.0 (d), 106.9.0 (d), 126.4 (d), 128.5 (d), 138.5(s), 140.6 (s), 141.7 (s).

2-Phenyl-3-methyl-2-cyclopenten-1-one (11a). A mixture of **3a** (190 mg, 1.0 mmol), 1 N NaOH solution (2 mL), and EtOH (2 mL) was refluxed for 4 h, then poured into H_2O (10 mL), extracted with CH_2Cl_2 (2 × 10 mL), and dried (Na_2SO_4). Evaporation of the solvent gave an oil, which was subjected to column chromatography on silica gel (5:1 hexane/EtOAc) to afford **11a** (162 mg, 94%) as a colorless oil. IR (neat) 1700, 1637, 1599, 1496 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.18 (s, 3H, 2H), 2.55 (m, 2H), 2.65 (m, 2H), 7.34−7.25 (m, 3H), 7.40 (t, $J = 7.4$ Hz); ^{13}C NMR (100 MHz) δ 18.3 (q), 31.8 (t), 34.8 (t), 127.6 (d), 128.3 (d), 129.1 (d), 131.8 (s), 140.4 (s), 171.8 (s), 207.6 (s). The IR and NMR spectra were identical with the reported data.[31]

2-(4-Bromophenyl)-3-methyl-2-cyclopenten-1-one (11b). A similar treatment of **3c** (538 mg, 2.0 mmol) produced **11b** (307 mg, 61%) as a colorless oil (column chromatography on silica gel eluted with 3:1 hexane−EtOAc). Bp 144 °C/0.9 mmHg; IR (neat) 1701, 1636, 1588, 1487 cm^{-1}; ^{1}H NMR (270 MHz) δ 2.16 (s, 3H), 2.54 (m, 2H), 2.64 (m, 2H), 7.16 (d, $J = 8.2$ Hz, 2H), 7.52 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (68 MHz) δ 18.2 (q), 31.8 (t), 34.6 (t), 127.4 (s), 128.1 (s), 130.7 (d), 131.3 (d), 139.1 (s), 172.2 (s), 207.1 (s); EI-MS *m*/*z* (rel intensity) 252 (M^+, 98), 250 (M^+, 100), 171 (37), 143 (73), 128 (99), 115 (64), 99 (100), 71 (7); HRMS calcd for $C_{12}H_{11}BrO$ 249.9993, found 249.9996.

Acknowledgment. We thank Mr. Takashi Nishimura (UBE Industries, Ltd.) for helpful suggestions and Prof. Norio Miyaura (Hokkaido University) for valuable discussions.

JO035468+

(37) Bowles, T.; Jones, R.; Porter, A. E. A.; Rechka, J. A.; Rzepa, H. S.; Williams, J. D. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1023.