A Straightforward Synthesis of Cyclobutenones via a Tandem Michael Addition/Cyclization Reaction of 2,3-Allenoates with Organozincs

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S *Supporting Information*

ABSTRACT: An efficient method for synthesis of poly-substituted cyclobutenones, which are not readily available from traditional methods due to the intrinsic ring strain, is described. The reaction of 2,3-allenoates and organozinc reagents proceeds via a tandem Michael addition/cyclic 1,2-addition/elimination mechanism with the functional groups from the organozinc reagents being introduced to the 3-position of the cyclobutenone products regiospecifically in moderate to excellent yields. Application to the synthesis of stereodefined β,γ-unsaturated enones is demonstrated.

Scheme 1. Known Methods and Concept for the Synthesis of Cyclobutenones from Allenoates

Cyclobutenones and their derivatives are not readily available due to their unique structures bearing the carbon−carbon double bond and carbonyl group in the strained four-membered rings.[1] However, they are important building blocks for the preparation of α,β-butenolides,[2a] cyclopentones,[2a] 1,3-dienes,[2b] and a variety of substituted cyclobutene derivatives. In addition, attention has been focused on their thermal reactivity[3] and transition metal-catalyzed reactions providing diversified ring-expanded compounds.[4] Cyclobutenones derivatives have also served as selective and orally active COX-2 inhibitors.[5] In the past years, the synthesis of such type of compounds is usually accomplished by [2+2] cycloadditions of acetylene with ketene[6] or keteniminium salt[7] (Scheme 1), which requires preformation of unstable ketene precursor and suffers from the limitation of the substituents on the four-membered ring and the regioselectivity referred to the alkynes. In principle, intramolecular reaction of the allylic C−M bond with the ethoxycarbonyl group in the **B**-type intermediate[8] (Scheme 1) would be a very convenient way to synthesize such compounds. However, due to the presence of strained cyclic ring and the difficulty in formation of the stereodefined **B** intermediate, it would be a great challenge to realize such a cyclization reaction.[9] Here we present our recent realization of such a concept by using readily available 2,3-allenoate[10] with organozincs as the starting materials.

After many trials and errors, we were pleased to find that the reaction of methyl 2-butyl-4-propyl-2,3-heptadienoate **1a** with diethyl zinc in toluene at room temperature afforded the desired product, 2-butyl-3-ethyl-4,4-dipropylcyclobut-2-enone **2a**, in 40% yield, with a recovery of 35% of the starting **1a**. The addition of some transition metal catalysts afforded poor results (entries 2−5, Table 1). Fortunately, we found that the reaction was significantly accelerated at an elevated temperature of 100 °C (entry 6). Study on solvent effect revealed that toluene and *n*-hexane are the best (compare entries 7−9, 11 with entries 6 and 10). However, the reaction in *n*-hexane is relatively slow (entry 10). Therefore, we
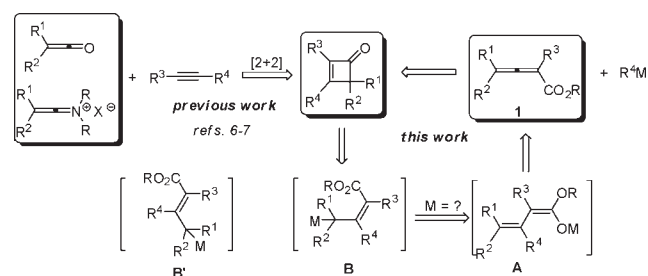
Table 1. Effects of Catalyst, Temperature, and Solvent on the Michael Addition/Cyclization of 2,3-Allenoate with Et$_2$Zn

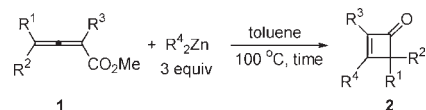| entry	solvent/ temp/time (h)	cat. (5 mol %)	yield[a] (%)		recovery of 1a[a] (%)
			2a	**3a**	
1	toluene/rt/14	—	40	10	35
2	toluene/rt/24	Fe(acac)$_3$	34	7	20
3	toluene/rt/24	CuCl	53	6	25
4	toluene/rt/24	CuCl$_2$	32	5	39
5	toluene/rt/13	Ni(PPh$_3$)$_2$Cl$_2$	6	9	48
6	**toluene/100 °C/1.5**	**—**	**95**	**1.5**	**1**
7	Et$_2$O/rt/19	—	32	20	48
8	CH$_3$CN/60 °C/13	—	0	2.5	97
9	THF/70 °C/18.5	—	58	8	19
10	*n*-hexane/60 °C/14	—	96	2	0.4
11	dioxane/100 °C/1.5	—	53	0.8	44

[a] Determined by NMR using dibromomethane as internal standard.

defined the reaction of 2,3-allenoates with 3 equiv of diethyl zinc in toluene at 100 °C as the standard reaction conditions (entry 6).

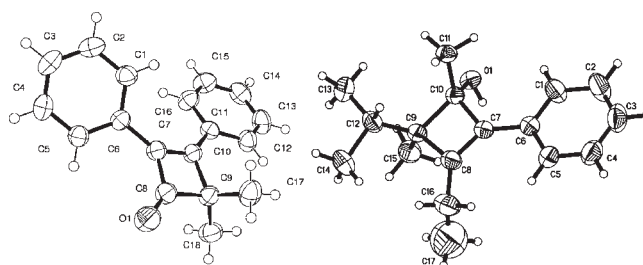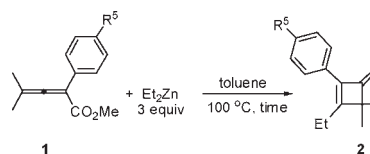The scope of this transformation was investigated under the standard conditions (Table 2). The reaction of a variety of fully

Table 2. Tandem Reaction of 2,3-Allenoates 1 with Orangozinc Reagents Affording Diversified Polysubstituted Cyclobutenones 2[a]

$$\underset{\underset{R^2}{\overset{R^1}{\diagup}}=\bullet\underset{CO_2Me}{\overset{R^3}{\diagup}}}{1} + R^4{}_2Zn \xrightarrow[\text{100 °C, time}]{\text{toluene}} \underset{R^4 \;\; R^1}{\overset{R^3 \quad O}{\square}} R^2$$

$$\text{1} \qquad \text{3 equiv} \qquad\qquad \text{2}$$

entry	R^1	R^2	R^3	R^4	time	isolated yield of 2 (%)
1	n-Pr	n-Pr	n-Bu (1a)	Et	1.5 h	70 (2a)
2	n-Pr	Me	n-Bu (1b)	Et	1.5 h	78 (2b)
3	i-Pr	Me	n-Bu (1c)	Et	1.5 h	80 (2c)
4[b]	t-Bu	Me	n-Bu (1d)	Et	4 h	74 (2d)
5	Me	Me	Ph (1e)	Et	3.5 h	72 (2e)
6	i-Pr	Me	Ph (1f)	Et	3.5 h	78 (2f)
7	Me	Me	p-FC$_6$H$_4$ (1g)	Et	1.5 h	72 (2g)
8	Me	Me	1-naphthyl (1h)	Et	2 h	79 (2h)
9	-(CH$_2$)$_4$-		t-Bu (1i)	Et	1 h	92 (2i)
10	-(CH$_2$)$_5$-		Ph (1j)	Et	1.5 h	88 (2j)
11	n-Bu	H	n-Bu (1k)	Et	10 min	50 (2k)
12	n-Bu	H	t-Bu (1l)	Et	20 min	90 (2l)
13	n-Pr	n-Pr	n-Bu (1a)	i-Pr	2 h	82 (2m)
14	n-Bu	H	t-Bu (1l)	i-Pr	0.5 h	80 (2n)
15[c]	Me	Me	p-FC$_6$H$_4$ (1g)	i-Pr	3.5 h	72 (2o)
16[c]	-(CH$_2$)$_5$-		Ph (1j)	i-Pr	2 h	74 (2p)
17	n-Pr	n-Pr	n-Bu (1a)	Ph	3 h	69 (2q)
18	n-Bu	H	t-Bu (1l)	Ph	0.5 h	82 (2r)
19	Me	Me	Ph (1e)	Ph	1.5 h	89 (2s)
20	-(CH$_2$)$_5$-		Ph (1j)	Ph	2.5 h	81 (2t)
21[d]	n-Pr	n-Pr	n-Bu (1a)	Et	2 h	68 (2a)

[a] The reaction was conducted with 0.4 mmol of 2,3-allenoates, 5 mL of toluene, and 3 equiv of R$^4{}_2$Zn (1.5 M solution in toluene for Et$_2$Zn, 1.0 M solution in toluene for i-Pr$_2$Zn, or pure Ph$_2$Zn); the formation of 1−9% hydrolysis product 3 was observed by ^{1}H NMR analysis of the crude reaction mixture. [b] The reaction was conducted in xylenes at 140 °C for a complete conversion. [c] The yield of hydrolysis product 3 is 12%. [d] The reaction was conducted with a 5.0 mmol scale of 1a.

Figure 1. ORTEP representation of 2s and trans-4e (right).

Table 3. Reaction of 2,3-Allenoates 1 with Functional Groups[a]

$$\underset{\underset{CO_2Me}{\diagup}}{\overset{R^5}{\bigcirc}} + Et_2Zn \xrightarrow[\text{100 °C, time}]{\text{toluene}} \underset{Et}{\overset{R^5}{\bigcirc}}$$

$$\text{1} \qquad \text{3 equiv} \qquad\qquad \text{2}$$

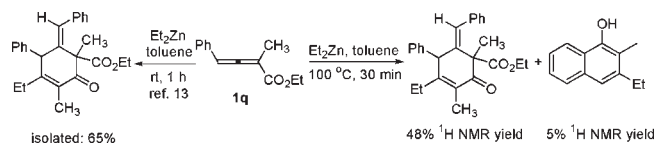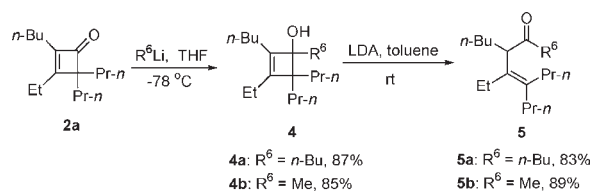| entry	R^5	time (min)	isolated yield of 2 (%)
1	Br (1m)	90	62 (2u)
2	CN (1n)	15	73 (2v)
3	CO$_2$CH$_3$ (1o)	15	75 (2w)
4	COCH$_3$ (1p)	15	45 (2x)

[a] The reaction was conducted with 0.4 mmol of 2,3-allenoates, 5 mL of toluene, and 3 equiv of Et$_2$Zn (1.5 M solution in toluene).

substituted 2,3-allenoates **1a−1j** and 4-monosubstituted 2,3-allenoates **1k−1l** with diethyl or diisopropyl zinc reagents afforded the corresponding cyclobutenones **2a−2p** in moderate to excellent yields (entries 1−16). Furthermore, diphenyl zinc can also be applied to the reaction affording **2q−2t** in good yields (entries 17−20). The substituents on the 4-position of the allenoates (R^1/R^2) can be H, and primary, secondary, and tertiary alkyl groups; the R^3 group could be alkyl and aromatic groups. When R^1 is a bulky alkyl group, i.e., tert-butyl group, the reaction needs to be conducted in xylenes at 140 °C to get a complete conversion probably due to the steric effect (entry 4). However, the reaction of substrates with bulky R^3 groups such as tert-butyl, phenyl, substituted phenyl, or naphthyl groups finished at 100 °C smoothly (entries 5−10, 12, 14−16, and 18−20). In addition, the reaction can be easily conducted at a scale of 5.0 mmol of the substrate **1a** in a similar yield (entry 21). The structure of the products was further confirmed by the X-ray single-crystal diffraction analysis of **2s** (Figure 1).[11]

Next, the functional group compatibility of this reaction was illustrated with substrates **1m−1p**. As shown in Table 3, Br and polar functional groups such as CN, CO$_2$CH$_3$, and COCH$_3$ were well tolerated under the standard conditions, affording the corresponding cyclobutenones **2u−2x** in 45−75% yields.

To unveil the mechanism, the reaction of substrate **1n** with Et$_2$Zn was carefully studied: the reaction proceeded smoothly even at room temperature within 5 min, however, affording the conjugate addition product **3b** upon protonolysis in 93% isolated yield.[12] Heating this resulting mixture at 100 °C led to the formation of cyclobutenone **2v** in 75% ^{1}H NMR yield, indicating the formation of **2v** via the intermediacy of **A1-Zn** (Scheme 2), although the cyclic 1,2-addition to the ester group to form the butenone ring is not easy.[13] The reaction of **1n** with EtMgBr was also examined: after formation of magnesium 1,3-dienolate **A1-Mg** under our previous conditions,[12] the reaction mixture was heated at 100 °C to afford a complicated mixture, instead of **2v** (Scheme 2), indicating the large difference of reactivities of the in situ formed Zn and Mg intermediates.

As in our previous study, control experiment showed that the reaction of 4-phenyl-substituted substrate **1q** with Et$_2$Zn at rt yielded (Z)-5-benzylidenecyclohex-2-enones,[13] while the same reaction at 100 °C afforded a mixture of (Z)-5-benzylidenecyclohex-2-enones[13] and naphthols[14] (Scheme 3). Here, the phenyl group on the 4-position may increase the reactivity of **B**-type intermediate toward the second molecule of 2,3-allenoate to trigger the second Michael addition and cyclization at room temperature, affording the (Z)-5-benzylidenecyclohex-2-enones; for the formation of the naphthol derivative at 100 °C, the phenyl group on the 4-position is directly involved after conjugate addition.[14]

In order to show new applications of this type of four-membered products,[2−4] the not readily available polysubstituted β,γ-unsaturated enones **5**[15,16] have been prepared from **2** and lithium reagents. 1,2-Addition of alkyl lithium reagents with **2a** afforded cyclobutenols **4a** and **4b**. Subsequent ring-opening of **4** in the presence of LDA afforded β,γ-unsaturated enones **5a** and **5b** in 83% and 89% yields, respectively (Scheme 4).[17]

Scheme 2. Control Experiments of 1n with Et$_2$Zn or EtMgBr at Different Temperatures
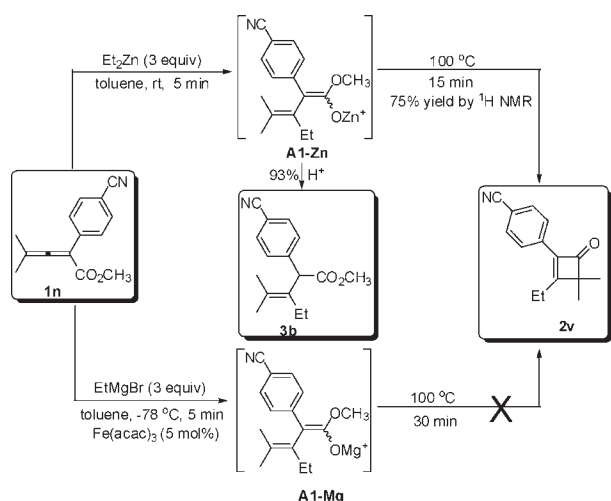
Scheme 3. Control Experiments of 1q with Et$_2$Zn under Different Conditions

Scheme 4. Synthesis of Polysubstituted β,γ-Unsaturated Enones 5

Table 4. 1,2-Addition of Organolithium Reagents with Cyclobutenones 2^{a,b}

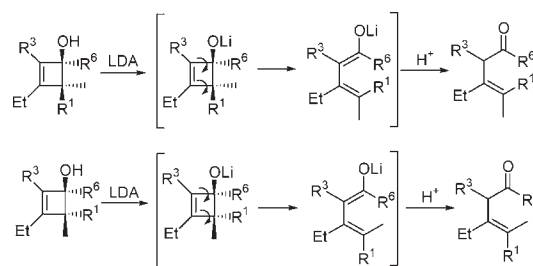|	**2**			isolated yield (%)	
entry	R^1/R^2/R^3	R^6	time (h)	cis-4	trans-4
1	Pr/Me/Bu (**2b**)	Bu	1	65 (cis-**4c**)	25 (trans-**4c**)
2	i-Pr/Me/Bu (**2c**)	Bu	0.5	76 (cis-**4d**)	9 (trans-**4d**)
3^c	i-Pr/Me/Ph (**2f**)	Me	4	70 (cis-**4e**)	13 (trans-**4e**)

^{a} 3 equiv of n-BuLi (2.5 M solution in n-hexane) or MeLi (1.3 M solution in Et$_2$O) were used. ^{b} In this table, Pr is n-propyl and Bu is n-butyl. ^{c} The reaction was conducted with 4 equiv of n-BuLi (2.5 M solution in n-hexane) in Et$_2$O for a better conversion of 93% (the conversion in THF was 69%).

Table 5. LDA-Promoted Ring-Opening Reaction of Cyclobutenols 4^a

entry	R^1	R^3	R^6	time (h)	isolated yield of **5** (%)
1	n-Pr	n-Bu	n-Bu (cis-**4c**)	3.5	91 (Z-**5c**)
2	i-Pr	n-Bu	n-Bu (cis-**4d**)	2	87 (Z-**5d**)
3^b	i-Pr	Ph	Me (cis-**4e**)	36	85 (Z-**5e**)
4	n-Pr	n-Bu	n-Bu (trans-**4c**)	4	87 (E-**5c**)
5	i-Pr	Ph	Me (trans-**4e**)	4	85^c (E-**5e**)

^{a} Single isomer was detected unless otherwise noted. ^{b} The reaction was conducted at −20 °C. ^{c} E/Z ≥ 98/2.

Scheme 5. Concerted Retro-4e-cycloaddition of Lithium 2-Cyclobutenoxides with Conrotation: An Explanation for the Stereochemistry Observed

When R^1 ≠ R^2 (R^1 > R^2), two stereoisomers, cis-**4** and trans-**4**, would form from the 1,2-addition reaction with cis-**4** being the major product due to the steric interaction between the incoming R^6 group from the lithium reagent and the bulky R^1 group. As expected, a bulkier substituent of R^1 leads to a better stereoselectivity (compare entry 1 with entry 2, Table 4). The configuration of the product was assigned by the X-ray single-crystal diffraction analysis of trans-**4e** (Figure 1).[18]

Excitingly, the LDA-promoted ring-opening reaction of cyclobutenols **4** was found to be highly stereoselective: the reaction of cis-**4** in the presence of LDA afforded corresponding Z-**5** exclusively in 85−91% yields, while the reaction of trans-**4** afforded corresponding E-**5** exclusively in 87% and 85% yields, respectively (entries 1−5, Table 5). The configuration of the carbon−carbon double bond was established by NOESY analysis.

The stereochemistry observed here is in accordance with the Woodward−Hoffmann rule, indicating that this opening reaction may involve a concerted retro-4e-cycloaddition of the lithium 2-cyclobutenoxides formed from the reaction of the alcohols with LDA (Scheme 5).

In summary, we have developed an efficient and general method to synthesize polysubstituted cyclobutenones, which are not readily

available from the traditional methods, in moderate to excellent yields. The products have been successfully applied to the highly stereoselective synthesis of poly substituted β,γ-unsaturated enones **5** in the presence of commercially available lithium reagents. Considering the easy availability and high functional group tolerance of organozinc reagent[19] and 2,3-allenoate,[20] this method will be of high interest in organic chemistry and related disciplines. Two interesting issues here are the highly stereoselective formation of **B**-type intermediate and the intramolecular 1,2-addition/elimination affording

the highly strained four-membered enones. Further study concerning on this issue is being conducted in our laboratory.

■ **ASSOCIATED CONTENT**

Ⓢ Supporting Information. Spectroscopic data, general procedure, and the $^1H/^{11}C$ NMR spectra of all the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ **ACKNOWLEDGMENT**

■ **REFERENCES**

(1) For reviews, see: (a) Wong, H. N. C.; Lau, K.-L.; Tam, K.-F. *Top. Curr. Chem.* **1986**, *133*, 83. (b) Belluš, D.; Ernst, B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 797. (c) Namyslo, J. C.; Kaufmann, D. E. *Chem. Rev.* **2003**, *103*, 1485.

(2) (a) Schmit, C.; Sahraoui-Taleb, S.; Differding, E.; Dehasse-De Lombaert, C. G.; Ghosez, L. *Tetrahedron Lett.* **1984**, *25*, 5043. (b) Murakami, M.; Miyamoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **2001**, *123*, 6441.

(3) For some representative examples, see: (a) Mayr, H. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 500. (b) Danheiser, R. L.; Gee, S. K. *J. Org. Chem.* **1984**, *49*, 1672. (c) Danheiser, R. L.; Gee, S. K.; Perez, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 806. (d) Perri, S. T.; Dyke, H. J.; Moore, H. W. *J. Org. Chem.* **1989**, *54*, 2032. (e) Enhsen, A.; Karabelas, K.; Heerding, J. M.; Moore, H. W. *J. Org. Chem.* **1990**, *55*, 1177. (f) Sun, L.; Liebeskind, L. S. *J. Org. Chem.* **1995**, *60*, 8194. (g) Liu, F.; Liebeskind, L. S. *J. Org. Chem.* **1998**, *63*, 2835. (h) Harrowven, D. C.; Pascoe, D. D.; Guy, I. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 425. (i) Hachiya, I.; Yoshitomi, T.; Yamaguchi, Y.; Shimizu, M. *Org. Lett.* **2009**, *11*, 3266. (j) Zhao, Y.-L.; Yang, S.-C.; Di, C.-H.; Han, X.-D.; Liu, Q. *Chem. Commun.* **2010**, 7614.

(4) For some representative examples, see: (a) Huffman, M. A.; Liebeskind, L. S.; Pennington, W. T., Jr. *Organometallics* **1990**, *9*, 2194. (b) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 8617. (c) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1991**, *113*, 2771. (d) Huffman, M. A.; Liebeskind, L. S.; Pennington, W. T. *Organometallics* **1992**, *11*, 255. (e) Semmelhack, M. F.; Ho, S.; Cohen, D.; Steigerwald, M.; Lee, M. C.; Lee, G.; Gilbert, A. M.; Wulff, W. D.; Ball, R. G. *J. Am. Chem. Soc.* **1994**, *116*, 7108. (f) Kondo, T.; Taguchi, Y.; Kaneko, Y.; Niimi, M.; Mitsudo, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 5369.

(5) Friesen, R. W.; Dubé, D.; Fortin, R.; Frenette, R.; Prescott, S.; Cromlish, W.; Greig, G. M.; Kargman, S.; Wong, E.; Chan, C. C.; Gordon, R.; Xu, L. J.; Riendeau, D. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2677.

(6) For reviews, see: (a) Hyatt, J. A.; Raynolds, P. W. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley: New York, 1994; Vol. 45, pp 179−186. (b) Tidwell, T. T. *Ketenes II*; Wiley: Hoboken, 2006. (c) Danheiser, R. L. In *Science of Synthesis: Houben Weyl Methods of Molecular Transformations*; Danheiser, R. L., Ed.; Thieme: Stuttgart, 2006; Vol. 23. (d) Danheiser, R. L.; Savariar, S.; Cha, D. D. *Org. Synth.* **1990**, *68*, 32. For some recent examples referring to the synthesis of cyclobutenones, see: (e) Kohnen, A. L.; Mak, X. Y.; Lam, T. Y.; Dunetz, J. R.; Danheiser, R. L. *Tetrahedron* **2006**, *62*, 3815. (f) Li, Z.; Moser, W. H.; Zhang, W.; Hua, C.; Sun, L. *J. Organomet. Chem.* **2008**, *693*, 361.

(7) Hoornaert, C.; Hesbain-Frisque, A. M.; Ghosez, L. *Angew. Chem., Int. Ed.* **1975**, *14*, 569.

(8) For a profile on the reaction of 1,3-dienolates **A**, see: (a) Fuson, R. C. *Chem. Rev.* **1935**, *16*, 1. (b) Denmark, S. E.; Heemstra, J. R., Jr.; Beutner, G. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 4682. (c) Zhao, D.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 14440.

(9) There are few reports on the intramolecular 1,2-addition/ elimination cyclization to form 4-membered cyclic products: (a) McGarvey, G. J.; Kimura, M. *J. Org. Chem.* **1985**, *50*, 4655. (b) Aidhen, I. S.; Ahuja, J. R. *Tetrahedron Lett.* **1992**, *33*, 5431. (c) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1993**, *58*, 7216. (d) Kise, N.; Agui, S.; Morimoto, S.; Ueda, N. *J. Org. Chem.* **2005**, *70*, 9407.

(10) For a $Co_2(CO)_8$-catalyzed transformation of ethyl 2,4,4-triphenyl-2,3-butadienoate to 3-ethoxy-2,4,4-triphenylcyclobutenone in 12% yield with 20% of conversion, see: Trifonov, L. S.; Orahovats, A. S.; Heimgartner, H. *Helv. Chim. Acta* **1987**, *70*, 1070.

(11) Crystal data for compound **2s**: $C_{18}H_{16}O$, MW = 248.31, monoclinic, space group $P2(1)/n$, final R indices $[I > 2\sigma(I)]$, R1 = 0.0386, wR2 = 0.1060, R indices (all data) R1 = 0.0432, wR2 = 0.1129, a = 9.0113(12) Å, b = 9.5129(12) Å, c = 16.236(2) Å, α = 90°, β = 96.700(4)°, γ = 90°, V = 1382.3(3) Å^3, T = 296(2) K, Z = 4, reflections collected/unique: 15462/2435 (R_{int} = 0.0222), number of observations $[>2\sigma(I)]$ 2163, parameters: 172. CCDC 800810.

(12) For our studies on the reaction of 2,3-allenoates with Grignard reagents affording conjugate addition products, see: (a) Lu, Z.; Chai, G.; Ma, S. *J. Am. Chem. Soc.* **2007**, *129*, 14546. (b) Lu, Z.; Chai, G.; Zhang, X.; Ma, S. *Org. Lett.* **2008**, *10*, 3517. (c) Chai, G.; Lu, Z.; Fu, C.; Ma, S. *Adv. Synth. Catal.* **2009**, *351*, 1946.

(13) Lu, Z.; Chai, G.; Ma, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 6045.

(14) Chai, G.; Lu, Z.; Fu, C.; Ma, S. *Chem.—Eur. J.* **2009**, *15*, 11083.

(15) The β,γ-unsaturated enones are important and versatile intermediates in organic synthesis and exist widely as functional groups in many natural products, see: (a) Thomas, A. F.; Thommen, W.; Willhalm, B.; Hagaman, E. W.; Wenkert, E. *Helv. Chim. Acta* **1974**, *57*, 2055. (b) Paterson, I.; Hulme, A. N. *Tetrahedron Lett.* **1990**, *31*, 7513. (c) Appendino, G.; Nano, G. M.; Viterbo, D.; De Munno, G.; Cisero, M.; Palmisano, G.; Aragno, M. *Helv. Chim. Acta* **1991**, *74*, 495. (d) Noda, Y.; Hashimoto, H.; Norizuki, T. *Heterocycles* **2001**, *55*, 1839.

(16) Due to the possible migration of the β,γ-C=C bond to the conjugated α,β-position, they are difficult to prepare. For some representatives on the synthesis of β,γ-unsaturated enones, see: (a) Cazes, B.; Julia, S. *Tetrahedron Lett.* **1974**, *15*, 2077. (b) Scarborough, R. M.; Smith, A. B. *Tetrahedron Lett.* **1977**, *18*, 4361. (c) Yano, K.; Baba, A.; Matsuda, H. *Chem. Lett.* **1991**, 1181. (d) Ma, S.; Shi, Z.; Li, L. *J. Org. Chem.* **1998**, *63*, 4522. (e) Schmieder-van de Vondervoort, L.; Bouttemy, S.; Padrón, J. M.; Bras, J. L.; Muzart, J.; Alsters, P. L. *Synlett* **2002**, 243. (f) Wang, S.-H.; Tu, Y.-Q.; Wang, M. *Tetrahedron Lett.* **2006**, *47*, 8621.

(17) There are two reports on the electrocyclic ring opening of cyclobutenone derivatives with lithium reagents, see cyclobutenone ethylenedithioacetals: (a) Regenhardt, W.; Schaumann, E.; Moore, H. W. *Synthesis* **2001**, 1076. Phenyl- and vinylcyclobutanones: (b) Ji, X.; Wang, Q.; Goeke, A. *Chem. Commun.* **2010**, 8845.

(18) Crystal data for compound *trans*-**4e**: $C_{17}H_{24}O$, MW = 244.36, triclinic, space group $P\bar{1}$, final R indices $[I > 2\sigma(I)]$, R1 = 0.0852, wR2 = 0.2450, R indices (all data) R1 = 0.1279, wR2 = 0.2840, a = 12.2850(8) Å, b = 16.5578(10) Å, c = 16.7837(8) Å, α = 74.767(5)°, β = 71.089(5)°, γ = 70.386(6)°, V = 2996.6(3) Å^3, T = 293(2) K, Z = 8, reflections collected/unique: 23881/10528 (R_{int} = 0.0541), number of observations $[>2\sigma(I)]$ 6270, parameters: 660. CCDC 800811.

(19) (a) Lorthiois, E.; Meyer, C. In *The Chemistry of Organozinc Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: Chichester, 2006; pp 863−977. (b) Knochel, P.; Leuser, H.; Gong, L.-Z.; Perrone, S.; Kneisel, F. F. In *Handbook of Functionalized Organometallics*; Knochel, P., Ed.; Wiley-VCH: Weinheim, Germany, 2005; pp 251−346. (c) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 6040.

(20) (a) Krause, N., Hashmi, A. S. K., Eds. *Modern Allene Chemistry*; WILEY-VCH: Weinheim, 2004; (b) Ma, S. *Chem. Rev.* **2005**, *105*, 2829.