Michael Addition of Acyclic Lithium 1,3-Dien-2-olates with α,β-Unsaturated Esters, Ketones, and Diesters

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The Michael addition of lithium 1,3-dien-2-olates with α,β-unsaturated carbonyl compounds is described. With α,β-unsaturated esters the reaction was reversible even at −78°C, while kinetically controlled with α,β-unsaturated ketones or alkylidenemalonates. At room temperature, the initially formed Michael adducts undergo subsequent intramolecular Michael addition to give substituted cyclohexanone derivatives in a highly stereoselective manner. Mostly *anti*-selectivity has been observed for the initial Michael addition, and the intramolecular cyclization was *cis*-selective.

1,3-Dien-1-olates, generated by the deprotonation of α,β-unsaturated carbonyl compounds, have enjoyed wide synthetic applications in alkylation,[1,2] acylation,[2c] aldol addition,[1d] Michael addition,[3,4] and other fields of organic synthesis.[5] Limited papers have been reported, however, about the reaction of 1,3-dien-2-olates; alkylation,[2,6a,b] aldol addition,[6c] and Michael addition[7] are among them. One exception is the cyclization reaction of cyclic 1,3-dien-2-olates with α,β-unsaturated esters or ketones. Since such reaction proceeds stereoselectively under mild reaction conditions to produce Diels–Alder type cyclization products, wide applications to natural product synthesis have been studied.[8]

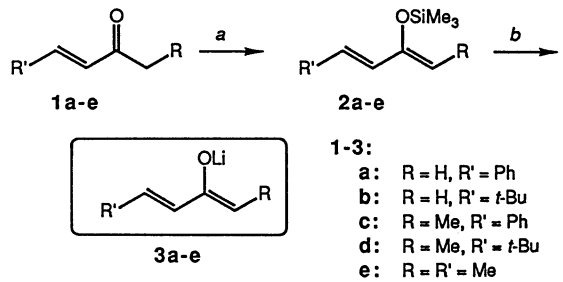
The *endo*-selectivities observed in these six-membered ring-forming reactions[7a,8,9] were the same as those of the *endo*-selective Diels–Alder reactions of related dienes such as cyclic 2-silyloxy-1,3-dienes.[10] This is why anion-accelerated Diels–Alder reaction is taken into account as a possible mechanism for the sequential double Michael reaction.[7a,8] Although there is known an example in which the Michael reaction between cyclic 1,3-dien-2-olates and α,β-unsaturated lactones resulted in a different stereoselectivity,[7b,c] high *endo*-selectivity is usually observed in the Michael addition of cyclic 1,3-dien-2-olates.

We assumed that the high stereoselectivity observed in the cyclization reaction of cyclic 1,3-dien-2-olates could be due to the attractive secondary orbital interaction just like the *endo*-selective Diels–Alder reaction. If this is true, such interaction would be generally utilized in the stereocontrol of Michael addition employing acyclic 1,3-dien-2-olates and α,β-unsaturated carbonyl compounds. In contrast with the many reported examples of *endo*-selective Diels–Alder type cyclization of cyclic 1,3-dien-2-olates, it is very surprising that few example is known for the Michael reaction of acyclic 1,3-dien-2-olates.[11]

Results and Discussion

Preparation of Lithium 1,3-Dien-2-olates. Lithium (1*Z*,3*E*)-1,3-dien-2-olates **3a**—**e** were generated from enones **1a**—**e** via 2-silyloxy-1,3-dienes **2a**—**e** as follows: Horner–Emmons olefination of 2-oxoalkylphosphonates using lithium bromide/triethylamine in tetrahydrofuran (THF) gave (*E*)-enones **1b**—**d** as single isomers (Scheme 1, **1b**: 71%, **1c**: 91%, **1d**: 78%); other enones **1a**,**e** were commercially available. Attempted lithiation of enones **1a**,**b** with lithium diisopropylamide (LDA) at −78 °C in THF produced the formal dimer[12] of **1** along with a complex mixture of many products,[13] indicating that the indirect generation method should be applied. Accordingly, enones **1a**—**e** were first silylated with chlorotrimethylsilane and 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU)[14] to give **2a**—**e** (**2a**: 71%, **2b**: 87%, **2c**: 64%, **2d**: 92%, **2e**: 78%) after vacuum distillation, among which **2c**—**e** were obtained as single isomers. Treatment of these 2-silyloxy-1,3-dienes **2a**—**e** with butyllithium,[3a] at room temperature for 30 min in THF generated lithium 1,3-dien-2-olates **3a**—**e** in excellent yields.

To determine the structure of **2d** by comparison with its stereoisomer **2d′**, silylation of **1d** was performed according to the Danishefsky's method[15] using chrolotrimethylsilane, triethylamine, and zinc chloride in benzene to produce an 89 : 11 mixture (GLC) of **2d** and **2d′** (Scheme 2); the major isomer **2d** was assigned the *Z*,*E*-isomer on the basis of NOE spectrum in which the



Scheme 1.

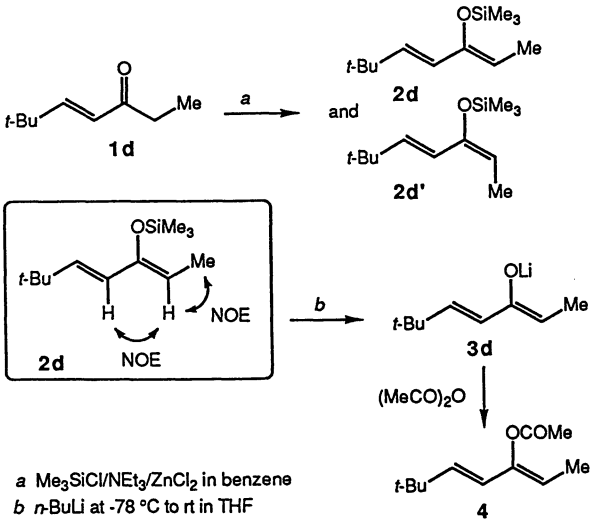
notable signal enhancement was observed between H-2 and H-4. Other 2-silyloxy-1,3-dienes **2c,e** were assigned also as the *Z,E*-structures by analogy.

Acetylation of **3d**, generated from **2d** and butyllithium by the method described above, with acetic anhydride gave acetate **4** in 85% yield as the sole *Z,E*-isomer, indicating the full retention of the *Z,E*-stereochemistry during the lithiation of **2d**. The use of THF containing hexamethylphosphoric triamide (HMPA, 10 vol%) as co-solvent in the above procedure provided essentially the equivalent result (**4**: 87%, single), confirming that the *Z*-isomer of **3d** is thermodynamically more stable.[16]

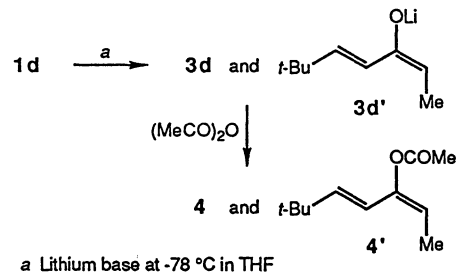
Direct lithiation of ethyl ketone **1d** with various lithium amides provided a mixture of isomeric lithium enolates, lithium *Z,E*-**3d** and *E,E*-enolate **3d'**. The *Z*/*E* ratios **3d**/**3d'** were determined after the mixtures of the lithium enolates **3d** and **3d'** were acetylated with acetic anhydride, while the yields of **4** were not always satisfactory (Scheme 3 and Table 1). The use of bulky lithium amides such as lithium hexamethyldisilylamide (LHMDS) and lithium 2,2,6,6-tetramethylpiperidide (LTMP), which are in general known to favor the formation of *E*-enolates, did not effect the selective generation of *E,E*-enolate **3d'**. The *Z,E*-isomer **3d** was still the major isomer (Table 1, Entries 6—9).[17]

Michael Reactions of Lithium 1,3-Dien-2-olates. Michael Addition to α,β-Unsaturated Esters. The reaction of lithium (2*Z*,4*E*)-6,6-dimethyl-2,4-heptadien-3-olate (**3d**) with methyl crotonate in THF was monitored on thin-layer chromatography (TLC). Within the reaction for 48 h at −78 °C, one clear new spot appeared and grew up along with the spot of **3d**, showing the occurrence of a clean reaction at a low temperature. Although this new spot was expected to correspond to the Michael adduct **6**, actually no trace of **6** was isolated after the usual hydrolytic quench of the reaction mixture. The starting enone **1d** was recovered quantitatively. Use of some other quenching agents such as saturated aqueous ammonium chloride, solid ammonium chloride, wet silica gel, methanol, *p*-toluenesulfonic acid, acetic acid, chlorotrimethylsilane, and iodomethane also resulted in the quantitative recovery of **1d**.

However, the cyclohexanone derivative **5a** was obtained in 49% yield as a single stereoisomer when the reaction temperature was raised to room temperature and continued for 26 h (Scheme 4 and Table 2, Entry 3). Assignment of the structure of **5a** will be discussed below. The stereoselective formation of **5a** seemed to



Scheme 2.



Scheme 3.

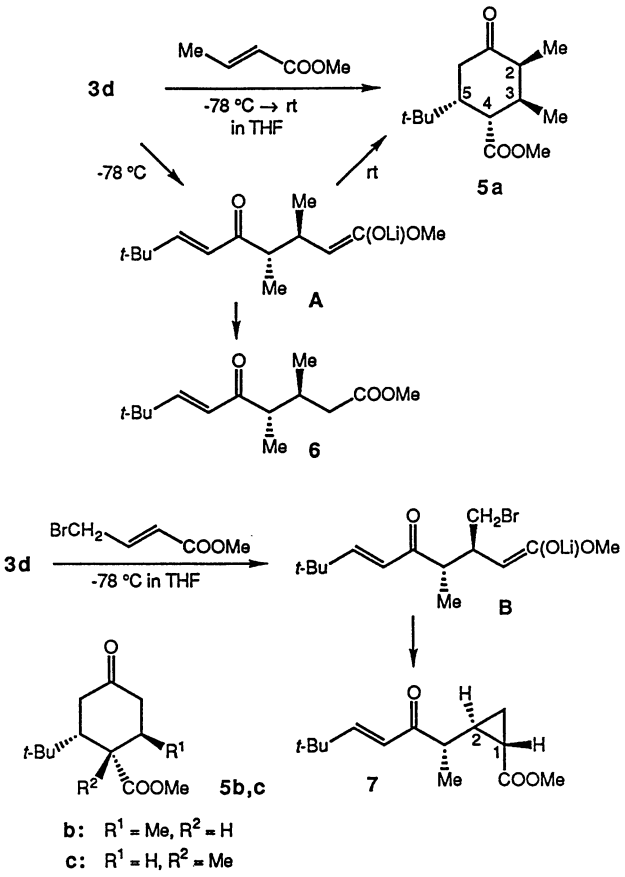
Table 1. Generation of 1,3-Dien-2-olates **3a**—**d**

Entry	Enone	Silyl enol ether (yield)	Lithium base	Lithium enolate	Isomer ratio (*Z*/*E*)[a]	Yield of **4**[b]
1	**1a**	**2a** (71%)	*n*-BuLi	**3a**	—	—
2	**1b**	**2b** (87%)	*n*-BuLi	**3b**	—	—
3	**1c**	**2c** (64%)	*n*-BuLi	**3c**	Single[c,d]	—
4	**1d**	**2d** (82%)	*n*-BuLi	**3d**	Single[d]	85
5	**1e**	**2e** (54%)	*n*-BuLi	**3e**	Single[c,d]	—
6	**1d**		LDA	**3d**	87:13	37
7	**1d**		LDA	**3d**	67:33[e]	51
8	**1d**		LHMDS	**3d**	88:12[e]	55
9	**1d**		LTMP	**3d**	67:33[e]	32

a) Determined by ^{1}H NMR spectrum after the *O*-acetylation with acetic anhydride. b) Isolated yield based on **2d** (Entry 4) or **1d** (Entries 6—9). c) The exclusive formation of (1*Z*,3*E*)-1,3-dien-2-olates was assumed on the basis of the observed full retention of Z,*E*-stereochemistry of the starting 2-silyloxy-1,3-diene **2d**. d) Pure (1*Z*,3*E*)-1,3-dien-2-olate. e) To the freshly prepared lithium bases in THF was added **1d** in a period of 25 min at −78 °C.

be deeply related with the appearance of a single spot on TLC during the aforementioned reaction at −78 °C. Employment of methyl (*E*)-4-bromo-2-butenoate, instead of methyl crotonate, in the reaction with **3d** at −78 °C in THF produced cyclopropane **7** as a single stereoisomer in 50% yield. It is clear that the formation of **7** took place through the intramolecular alkylation of the stereoselectively formed Michael adduct enolate **B**.

The following points are clear on the basis of these results: (1) the Michael addition of **3d** with methyl crotonate is a reversible process,[18] (2) As readily anticipated from the decreased length of conjugation, the Michael adduct enolate **A** is less stabilized than the starting enolate **3d** so that the equilibrium lies in favor for **3d**, (3) the adduct enolate **A** rapidly decomposes into each components on quenching, (4) the irreversible cyclization of the minor contributor **A** takes place around room temperature to produce the cyclized product **5a**, and (5) the reversible process and the irreversible cyclization are both stereoselective.



Scheme 4.

To stabilize the Michael adduct enolate **A**, the lithium enolate **3d** was first treated with zinc(II) chloride[19] at −20 to −30 °C and then allowed to react with methyl crotonate at room temperature[20] to give the Michael adduct **6** as a single diastereomer, albeit in a low yield (18%). Based on the reversible nature of the reported aldol reaction of zinc enolates with carbonyl compounds,[21] it is likely that the Michael reactions of lithium enolate **3d** and its zinc derivative are both reversible. The *anti*-configuration of **6** was tentatively assigned on the basis of the structure of **5a** which was derived from **A** presumably under thermodynamic control.

Similar reactions of lithium (1*Z*,3*E*)-5,5-dimethyl-1,3-hexadien-2-olate (**3d**) with methyl crotonate (4 h) and methacrylate (15 h) at room temperature produced cyclohexanone derivatives **5b** (87%) and **5c** (20%), respectively, both as single stereoisomers again (Scheme 4 and Table 2, Entries 1, 2).

The skeletons of **5a**—**c** correspond to the formal Diels–Alder cycloadducts of lithium 1,3-butadien-2-olates **3b,d** with methyl crotonate and methacrylate.[10] With an expectation to obtain the corresponding Diels–Alder cycloadduct, whose stereostructure may be readily assigned on the basis of the well-established stereochemical dignity of Diels–Alder reaction, enone **2d** was heated with methyl crotonate in benzene at 130 °C in a sealed tube for 6 d. However, the quantitative recovery of **2d** resulted, and the stereostructures of **5a**—**c** were assigned only on the spectroscopic basis.

The most bulky *t*-butyl substituent of **5a** must occupy the equatorial position in its stable chair conformation. That the axial H-5 showed only one big vicinal coupling with H-6$_{ax}$ (J_{5-6ax}=14.3 Hz) and the other two couplings were small (J_{5-6eq}=4.0 and J_{5-4}=3.8 Hz) indicates the 4,5-*cis* relationship. Notable NOEs were observed between H-6$_{ax}$/H-2 and H-2/H-3, showing the axial and equatorial positions of H-2 and H-3, respectively. Thus, **5a** was determined as *r*-2,*c*-3,*t*-4,*t*-5-configuration. Similar structural analysis was applied to **5b** (Scheme 4).

Table 2. Reiterative Michael Addition of Lithium 1,3-Dien-2-olates **3** with α,β-Unsaturated Esters

Entry	Enolate	α,β-Unsaturated ester	Solvent	Temp/°C[a]	Time/h[a]	Product	Yield/%[b]	Isomer ratio[c]
1	**3b**	Methyl crotonate	THF	−78→rt	2.3→1.5	**5b**	87	Single
2	**3b**	Methyl methacrylate	THF	−78→rt	2.5→22	**5c**	20	Single
3	**3d**	Methyl crotonate	THF	−78→rt	1.5→26	**5a**	49	Single
4	**3d**[d]	Methyl crotonate	THF	−78→rt	20→52	**6**	18	Single
5	**3d**	Methyl 4-bromocrotonate	THF	−78	17	**7**	50	Single

a) Each reaction time corresponds to each reaction temperature. b) Isolated yield based on **2**. c) Based on ^{1}H NMR spectrum. d) The lithium enolate **3d** was treated with zinc(II) chloride (1 equiv) at −20 to −30 °C for 20 min before methyl crotonate was added.

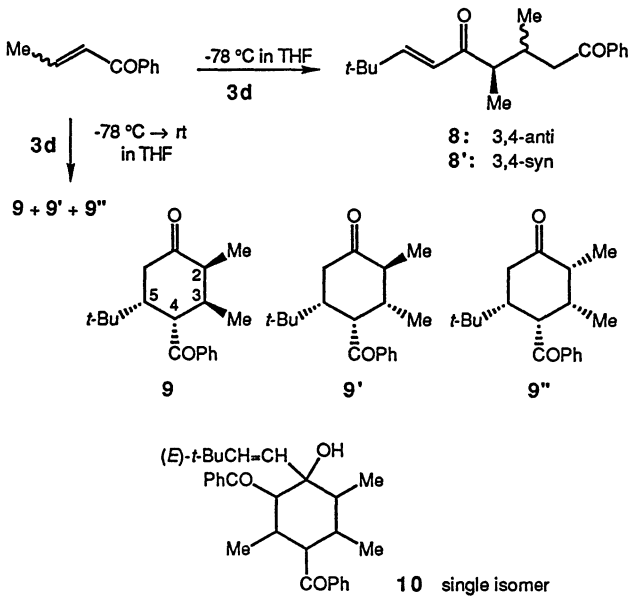
Structure assignment of **5c** was mainly based on the analogy of reaction mode to that of the above two cases.

As a result, the reaction of (1*Z*,3*E*)-1,3-dien-2-olate **3d** with methyl crotonate led to the stereoselective formation of *anti*-adduct enolate **A**, which was in an equilibrium with the starting components, **3d** and methyl crotonate. Stereoselectivity in the retro-Michael reaction process is not important because thermodynamically more stable *Z*-enolate **3d** and methyl crotonate are released from **A** in this retro process, and hence the retro Michael reaction process would not affect the stereoselectivity of the whole reaction. The 4,5-*cis*-selective intramolecular Michael addition pathway from the initially formed *anti*-Michael adduct enolates **A** leading to **5a—c** corresponds to that observed previously in the second cyclization step of the Michael addition of cyclic 1,3-dien-2-olates.[8] Probably the role of metal chelation is important.[9,22]

Although the *trans*-substitution of the cyclopropane ring of **7** was determined by its small vicinal coupling constant between H-1/H-2 (J_{1-2}=4.4 Hz), the configuration at the third chiral center could not be assigned only on the spectroscopic basis. Since *anti*-adduct enolate **A** was confirmed to be the intermediate involved in the reaction of **3d** with methyl crotonate, a similar *anti*-adduct enolate **B** was proposed as the intermediate involved in this reaction. Stereochemistry of **7** was tentatively assigned as shown in Scheme 4.

Michael Addition to 1-Phenyl-2-buten-1-one, (*E*)-3-Penten-2-one, or (*E*)-4-Phenyl-3-buten-2-one. To suppress the retro-Michael reaction pathway, α,β-unsaturated ketones were employed as Michael acceptors in the reactions with 1,3-dien-2-olate **3d**. Stabilization of a carbanionic center by the attaching α-acyl substituent is much higher than the stabilization by the α-ester moiety. As expected, a smooth Michael reaction took place between **3d** and 1-phenyl-2-buten-1-one ($Z:E$=10:90 by ^{1}H NMR) in THF; this reaction was completed in 1 h at −78 °C. An 87:13 mixture (^{1}H NMR) of Michael adducts **8** and **8′** was obtained in 73% of combined yield, after quenching with *p*-toluenesulfonic acid (Scheme 5, Table 3, Entry 1).

It was clear by the following observation that no retro-Michael reaction took place in the stage of



Scheme 5.

Table 3. Reaction of Enolate **3d** and/or **3d′** with 1-Phenyl-2-buten-1-one

Entry	1-Phenyl-2-buten-1-one *Z*/*E*	Dienolate[a] **3d**/**3d′**	Solvent/additive[b]	Temp °C	Time h	Product	Yield[c] %	Isomer ratio[d] *anti*/*syn*
1	10:90	**3d**	THF	−78	1	**8**+**8′**	73	87:13
2	9:91	**3d**	THF/HMPA	−78	0.5	**8**+**8′**	84	95:5
3	9:91	**3d**	THF/18-Crown-6	−78	2.5	**8**+**8′**	81	95:5
4	1:99	**3d**	THF	−78	0.5	**8**+**8′**	83	85:15
5	1:99	**3d**	THF/HMPA	−78	0.5	**8**+**8′**	87	95:5
6	99:1	**3d**	THF	−78	1	—		
7	99:1	**3d**	THF/HMPA	−78	1.5	—		
8	99:1	**3d**	THF	−78	18	**8**+**8′**	51	62:38
9	99:1	**3d**	THF/HMPA	−78	18	**8**+**8′**	50	59:41
10	1:99	**3d**+**3d′** (87:13)[e]	THF	−78	0.5	**8**+**8′**	87	78:22
11	1:99	**3d**+**3d′** (67:33)[f]	THF	−78	0.5	**8**+**8′**	72	67:33
12	1:99	**3d**+**3d′** (88:12)[g]	THF	−78	0.5	**8**+**8′**	75	89:11
13	1:99	**3d**+**3d′** (67:33)[h]	THF	−78	0.5	**8**+**8′**	57	58:42
14	1:99	**3d**+**3d′** (67:33)[e]	THF/HMPA	−78	0.5	**8**+**8′**	67	63:37
15	10:90	**3d**	THF	rt	42	**9**+**9′**+**9″**	71	62:16:22 (84:16)[i]
16	10:90	**3d**	THF/HMPA	rt	18	**9**+**9′**+**9″**	79	73:11:16 (89:11)[i]
17	99:1	**3d**	THF	rt	18	**9**+**9′**+**9″**	79	47:9:44 (91:9)[i]

a) Unless otherwise referred, enolates **3d** and **3d′** were generated from **2d** and LDA. b) HMPA (12 vol% to THF) or 18-cown-6 (1 equiv) was added as an additive. c) Isolated yield based on **2d** or **1d**. d) Determined by HPLC. e) Generated from **1d** and LDA. f) To the freshly prepared LDA in THF was added **1d** in a period of 25 min at −78 °C. g) Generated from **1d** and LHMDS. h) Generated from **1d** and LTMP. i) The calculated *anti*/*syn*-selectivity based on the ratios of **9**, **9′**, and **9″**.

Michael adduct formation at −78 °C as confirmed. Thus, when the Michael adduct enolate derived from **3d** and 1-phenyl-2-buten-1-one was treated with dimethyl ethylidenemalonate, no corresponding Michael adduct to the ethylidenemalonate acceptor was detected. The details of the reaction of **3d** with alkylidenemalonates will be described below. The Michael reaction of **3d** with 1-phenyl-2-buten-1-one (*Z*: *E*=1 : 99 to 9 : 91) in the presence of HMPA or 18-crown-6 showed satisfactorily high *anti*-selectivity (Table 3, Entries 2, 3, 5).

Next examined was the Michael reaction of (*E*)-1-phenyl-2-buten-1-one (99% pure) with the lithium 1,3-dien-2-olate with several **3d**/**3d′** ratios. As shown in Table 3 (Entries 10—13), the stereoselectivity **8**/**8′** was related with the enolate ratio **3d**/**3d′**, *anti*- **8** and *syn*-adduct **8′** being formed mainly from the *E*- and *Z*-enolate, respectively. Addition of HMPA increased the *anti*-selectivity, but only by 5% (Entry 14), making a striking contrast with the highly *anti*-selective Micahel addition of **3d** (Entries 2,5).

On the other hand, (*Z*)-1-phenyl-2-buten-1-one[23] was found to be much less reactive toward **3d**. No formation of the Michael adduct was detected on TLC after 1 h at −78 °C (Entry 6); addition of HMPA to activate the enolate **3d** was also totally ineffective (90 min at −78 °C, Entry 7). Finally, (*E*)-1-phenyl-2-buten-1-one was added to this reaction mixture and allowed to react for additional 1 h to give an 83 : 17 mixture of **8** and **8′** (65%) along with the single stereoisomer of the cyclized product **10** (28%), whose stereochemistry remained unsolved. Thus, the diastereomer ratio **8**/**8′** was independent of the *Z*/*E* ratio of the acceptor molecule, 1-phenyl-2-buten-1-one (Table 3, Entries 1—5). This is because (*E*)-1-phenyl-2-buten-1-one was the only reactive isomer. The lack of full conjugation between the carbon–carbon double bond and the carbonyl moiety may be the major reason for the decreased reactivity of (*Z*)-1-phenyl-2-buten-1-one.

When the reaction time was prolonged, (*Z*)-1-phenyl-2-buten-1-one reacted with **3d** at −78 °C to give a mixture of **8** and **8′** albeit in a poor isomer ratio (**8** : **8′**=62 : 38, Entry 8); essentially the equivalent result (**8** : **8′**=59 : 41, Entry 9) was obtained in a similar reaction in the presence of HMPA. The low *anti*-selectivity in the presence of HMPA and no dramatic change of the isomer ratio were again surprising. Although the products obtained were in cyclized forms, high stereoselectivity and satisfactory yield were observed when the same reaction was carried out at room temperature (Entry 17, 91 : 9). The poor *anti*/*syn*-selectivity observed in the reactions at −78 °C would be due to the slow Michael addition of (*Z*)-1-phenyl-2-buten-1-one. This *Z*-isomer presumably underwent partial isomerization to (*E*)-1-phenyl-2-buten-1-one in the course of Michael addition through the retro-Michael addition pathway.

At room temperature, three isomers of the cyclized products **9**, **9′**, and **9″** were obtained in the reaction of **3d** with (*Z*)-1-phenyl-2-buten-1-one (Entry 17). Since these products were assigned, mainly on the basis of NOE spectra, *r*-2,*c*-3,*t*-4,*t*-5- for **9**, *r*-2,*t*-3,*t*-4,*t*-5- for **9′**, and *r*-2,*c*-3,*c*-4,*c*-5-isomer for **9″**, the stereoselectivity of the intermolecular Michael addition was calculated to be *anti*/*syn*=91 : 9. The reactions with (*E*)-1-phenyl-2-buten-1-one at room temperature afforded the comparable results (Entries 15, 16). The equally high *anti*-selectivities observed in these reactions (Entry 17 and Entries 15, 16), regardless of the *Z*/*E* ratio of the acceptor molecules employed, would be due to the ready isomerization of (*Z*)-1-phenyl-2-buten-1-one to the (*E*)-1-phenyl-2-buten-1-one at room temperature.

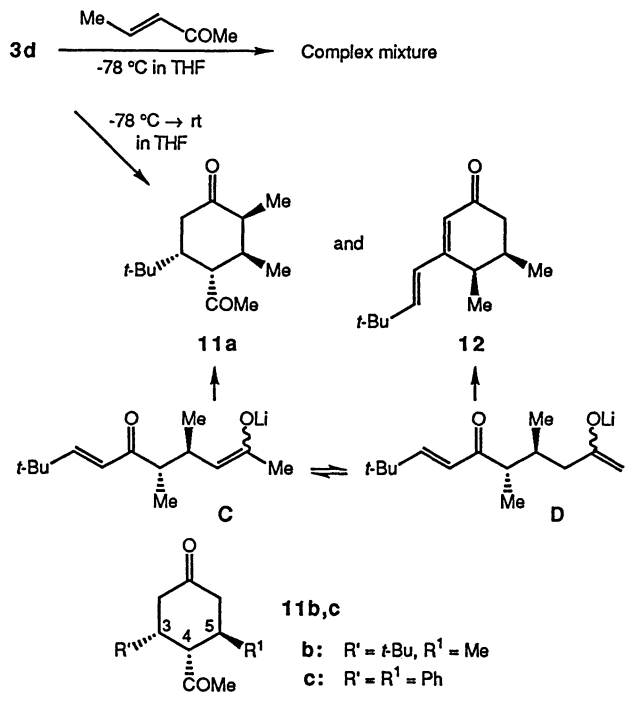
Stereostructures of the cyclized products, **9** and **9′**, were determined on the basis of ^{1}H NMR spectra: Based on the small couplings for J_{5-4}(4.0 Hz) and J_{2-3}(6.2 Hz) as well as the notable NOEs between H-2/H-3, H-2/H-6$_{ax}$, and H-5/3-Me, the major stereoisomer **9** was confirmed to be the 2,3-*cis*-3,4-*trans*-4,5-*cis* structure. On the other hand, the small coupling for J_{5-4}(3.7 Hz) and big coupling for J_{2-3}(12.4 Hz) indicated the axial positions of H-2, H-3, and H-5 and the equatorial position of H-4, minor isomer **9′** being assigned the 2,3-*trans*-3,4-*cis*-4,5-*cis* structure.

The points to be noteworthy are: (1) at a low temperature (−78 °C) *anti*-**8** and *syn*-Michael adduct **8′** are mainly formed from (2*Z*,4*E*)-**3d** and (2*E*,4*E*)-1,3-dien-2-olate **3d′**, respectively, (2) the stereospecific cyclization of the resulting Michael adduct enolates leads to the cyclization products **9** and **9′** at room temperature, (3) the Michael addition at a low temperature is kinetically controlled, (4) (*Z*)-1-phenyl-2-buten-1-one is much less reactive than the (*E*)-1-phenyl-2-buten-1-one in the reaction with **3d**, (5) the presence of HMPA does not alter the transition state, (6) the fast retro process is involved in the reaction at room temperature, while this process is less important at −78 °C.

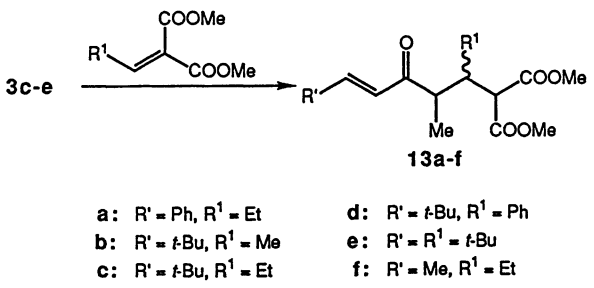
The reaction of lithium (1*Z*,3*E*)-1,3-dien-2-olate **3d** with (*E*)-3-penten-2-one at room temperature produced two cyclized products **11a** and **12** in 5 and 49% yields, respectively, while the same reaction at −78 °C resulted in the formation of complex products (Scheme 6). The structures of **11a** and **12** were determined on the basis of spectral data and also of the assumed reaction mode, and the 4,5-*cis*-configuration of **12** was confirmed by the small J_{4-5} value (3.7 Hz). The initial *anti*-Michael adduct enolate **C** went to the equilibration with the terminal enolate **D** whose irreversible aldol condensation produced **12**. Slow cyclization of enolate **C** into **11a**, even at room temperature, probably allowed the equilibration with **D**.

Similarly, reactions of **3b** and **3a** with (*E*)-3-penten-2-one and (*E*)-4-Phenyl-3-buten-2-one at room temperature gave stereoselectively cyclized products **11b** (31%) and **11c** (31%), respectively.

Michael Addition to Alkylidenemalonates. As discussed above, the reactions of lithium 1,3-dien-2-olates **3** with α,β-unsaturated esters were thermodynamically



Scheme 6.



Scheme 7.

controlled even at −78 °C, no Michael adducts having been isolated on quenching. Although α,β-unsaturated ketones and **3** formed stable adducts at a low temperature (−78 °C), they underwent ready equilibration with the starting substrates at room temperature. On the other hand, alkylidenemalonates bear two electron-withdrawing ester groups at the same sp^2 carbon so that high stabilization of the adduct enolates is expected. Therefore their Michael addition should be kinetically controlled.

One of two ester moieties of alkylidenemalonates is cis to the β-substituent R^1 and the other trans, and therefore the study of Michael addition of **3** with alkylidenemalonates would provide some useful informations to solve the transition state. The question on the aforementioned rate difference of Michael additions to the *Z*- and *E*-enone acceptors, e.g. (*Z*)- and (*E*)-1-phenyl-2-buten-1-one and that on the kinetic stereoselectivity of the *Z*- and *E*-isomers of α,β-unsaturated carbonyl acceptors would be also answered.

The reactions of **3c—e** with alkylidenemalonates went to full completion within 30 min at −78 °C to give, after usual hydrolytic workup, the corresponding Michael adducts **13a—f** in excellent yields (Scheme 7 and Table 4). One exception was the reaction with dimethyl (2,2-dimethylpropylidene)malonate bearing a bulky *t*-butyl β-substituent. A higher reaction temperature and a longer reaction time were required (11 days at room temperature) and the Michael adduct **13e** was obtained only in 36% yield (Entry 9). When the β-substituent R^1 of the alkylidenemalonates was small, e.g. R^1=Me or Et, the diastereomer ratios were extremely poor (70 : 30 to 52 : 48) regardless of the nature of the terminal substituent R′ of the donor molecules **3** (Entries 1—6, 10). On the other hand, selectivities better than 90% were achieved when a bulky β-substituent R^1 such as Ph or *t*-Bu was attached at the β-position (Entries 7—9). Improvement of the stereoselectivity by adding HMPA was observed, but again only a little (Entries 2, 4, 6, 8).

It was found that the reactions with alkylidenemalonates were all kinetically controlled on the basis of the following cross reaction. Treatment of the Micahel adduct enolate between **3d** and dimethyl propylidenemalonate with dimethyl ethylidenemalonate produced no adduct to the latter acceptor.

Stereochemistry of the major isomer of **13d** was determined by its chemical conversion shown in Scheme 8

Table 4. Reaction of Enolates **3** with Dimethyl Alkylidenemalonates

Entry	Dienolate 3	Alkylidenemalonate R^1	Solvent/additive[a]	Temp/°C	Time/h	Product	Yield/%[b]	Isomer ratio *anti*/*syn*[c]
1	**3c**	Et	THF	−78	0.5	**13a**	85	55 : 45
2	**3c**	Et	THF/HMPA	−78	0.5	**13a**	83	62 : 38
3	**3d**	Me	THF	−78	0.5	**13b**	83	52 : 48
4	**3d**	Me	THF/HMPA	−78	0.5	**13b**	87	60 : 40
5	**3d**	Et	THF	−78	0.5	**13c**	80	60 : 40
6	**3d**	Et	THF/HMPA	−78	0.5	**13c**	82	70 : 30
7	**3d**	Ph	THF	−78	0.5	**13d**	64	92 : 8
8	**3d**	Ph	THF/HMPA	−78	0.5	**13d**	89	95 : 5
9	**3d**	*t*-Bu	THF	rt	11d	**13e**	36	93 : 7
10	**3e**	Et	THF	−78	0.5	**13f**	60	64 : 36

a) HMPA (12 vol% to THF) was added as an additive. b) Isolated yield based on **2**. c) Determined by HPLC or ^{1}H NMR.

and also on the basis of spectral analysis of the derivatives. The 95:5 mixture of **13d** was purified through column chromatography to give pure sample of the major isomer of **13d**. Catalytic reduction of **13d** over palladium/carbon was followed by the carbonyl reduction with zinc borohydride in ether to give the expected lactone **15** (41%, 85:15) along with hemilactal **16** (37%, 76:24) as an overreduction product. Although these products **15** and **16** were derived from the diastereomeric alcohols produced from **14**, their different reactivity toward the zinc borohydride reduction is uncertain. It was clear that **15** consisted of two 3-epimers and **16** was a mixture of the 2- or 3-epimers, because they were converted into **17** and **18**, respectively, as single stereoisomers by the followed demethoxycarbonylation and oxidative demethoxycarbonylation. Thus, **15** and **16** were treated with aqueous sodium hydroxide in methanol at room temperature to give **17** (66%, single isomer) and **18** (94%, single isomer), respectively.

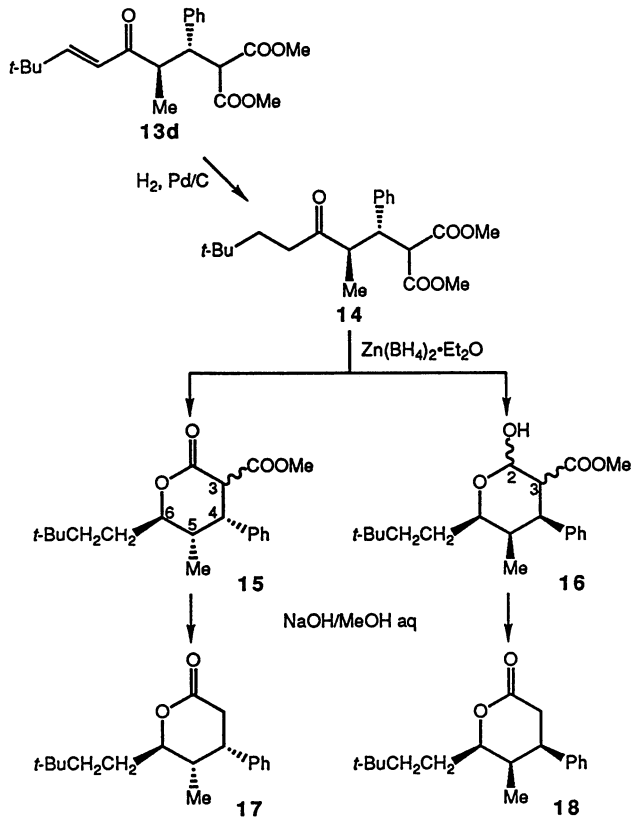
Structures of **17** and **18** were easily distinguished from each other on the basis of the observed NOE spectra (**17**: H-4/H-5, 4-Ph/5-Me, and 4-Ph/H-6; **18**: H-3_{ax}/Ph, H-3_{eq}/H-4, H-4/H-5, H-4/H-6, and H-5/H-6). Thus, the major isomer of **13d** was determined to be the *anti*-configuraion, and therefore the other major diastereoisomers **13a**—**f** obtained in the reactions of **3c**—**e** with alkylidenemalonates were assigned *anti*-stereochemistry by analogy.

Nature of Transition State. After the transition state model recently proposed by Heathcock and co-workers for the Michael addition of amide and thioamide enolates,[24] transition states **E**, **F**, **E′** and **F′** were drawn in Fig. 1. The reaction between **3d** and (*E*)-1-phenyl-2-buten-1-one was chosen as the representative example for the Michael addition of lithium 1,3-dien-2-olates to α,β-unsaturated carbonyl compounds.

From the viewpoint of stabilization of the chelating bond, the chelation between the lithium atom of **3d** and the carbonyl oxygen of the acceptor molecule should be most favorably built with the nonbonding orbital of the oxygen (models **E′** and **F′**). However, **E′** and **F′** were not the transition states actually involved in the reactions because there are serious steric repulsions between the *t*-butyl and the phenyl substituents (**F′**) or between the eclipsed three substituents (**E′**). The second favorable models were constructed with the pai orbital of the carbonyl moiety (models **E** and **F**).

The transition state **F** leading to the *syn*-adduct **8′** is nearly identical with **F′** where the only difference is the location of the lithium atom, and so **F** is also suffering from the serious steric repulsion. Without such steric repulsion between the *t*-butyl and phenyl substituents, **F** and **F′** should have been highly stabilized by chelate formation as well as the secondary orbital interaction that is often very important in the *endo*-transition state of Diels–Alder reaction. It was finally concluded that the anticipated transition state **F** or **F′** was not included in the Michael additions of lithium 1,3-dien-2-olates **3** to α,β-unsaturated carbonyl compounds. The participation of the sterically most favored transition state **E** led to the *anti*-adduct **8** as major diastereomers.

In the reaction of **3d** with alkylidenemalonates bearing a small β-substituent R^1, there are two possible



Scheme 8.

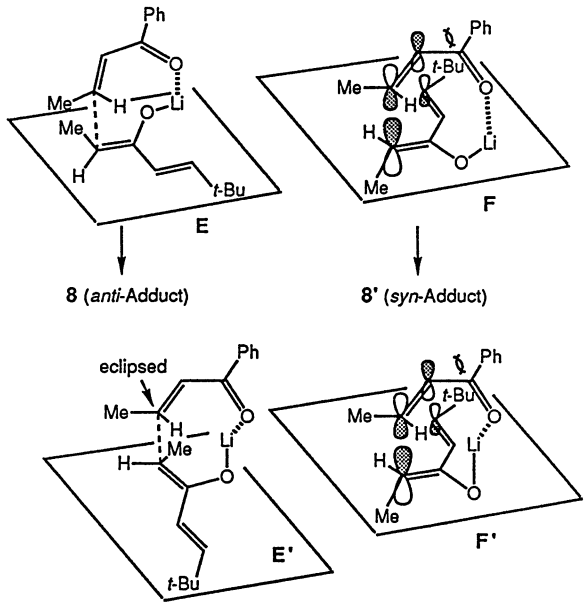


Fig. 1. Chelated treansition state for the Michael addition of lithium 1,3-dien-2-olate **3d** to (*E*)-1-phenyl-2-buten-1-one.

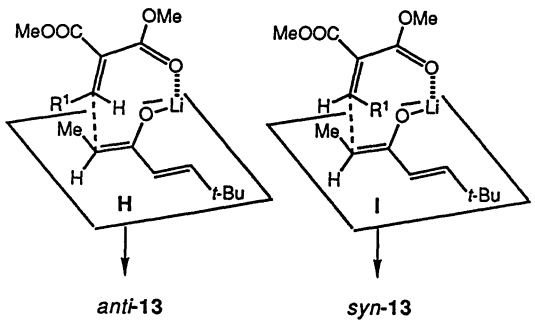


Fig. 2. Chelated transition state for the Michael addition of lithium 1,3-dien-2-olate **3d** to dimethyl alkylidenemalonates.

chelated transition states **H** and **I** with comparable stabilization energies (Fig. 2). When R^1 becomes bulky, the transition state model **I** becomes less favored sterically. Thus, it is now understood that poor stereoselectivities were observed in the reaction with the alkylidenemalonates bearing a small β-substituent R^1.

We assume that the role of chelate formation would be quite important in the Michael addition of lithium enolates to α,β-unsaturated carbonyl compounds. Little change of stereoselectivity by adding HMPA to the reaction system was observed throughout the present work. Although this seems to be inconsistent with the importance of chelation, an increased reactivity of the chelated acceptor molecule may be a key clue. The metal atom of the enolates would work as a Lewis acid catalyst to lower the LUMO (lowest unoccupied molecular orbital) level of the acceptor molecule when they come into chelation so that only the chelated acceptors are activated. The addition of a polar additive like HMPA to the reaction system does decrease the concentration of chelating molecules, but the chelating acceptors are preferentially allowed to undergo the Michael addition. There is no doubt that the reaction was chelation-controlled.

Experimental

General. Melting points were recorded on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with JASCO IRA-1 and A-702 spectrometers. ^{1}H and ^{13}C NMR spectra were measured with Hitachi R-40 (^{1}H NMR: 90 MHz) and JEOL GSX-270 (270 MHz for ^{1}H NMR and 67.94 MHz for ^{13}C NMR) instruments. Chemical shifts are recorded in parts per million downfield from internal tetramethylsilane. Mass spectra and high-resolution mass spectra (HRMS) were taken with a JEOL-01SG-2 spectrometer at an ionization energy of 70 eV. Elemental analyses were performed with a Hitachi 026 CHN analyzer. For preparative column chromatography, Wakogel C-200, C-300, and Merck silica gel 60 were employed. Flash chromatography was performed with an Eyera EF-10 apparatus with a 20×180 mm column packed with silica gel 60 (0.04—0.063 mm). Gas liquid chromatography (GLC) was accomplished with a Yanaco G-2800 gaschromatograph with an ionization flame detector using a 3×2000 mm glass column (SE-30) or a 0.25×50000 mm glass capillary column (Silicone GE, SE-30). Micro vacuum distillation was carried out on a Sibata GTO-250R Kugelrohr distilling apparatus.

Materials. Enones **1a** and **1e** are commercially available, and **1b**[25] and **1c,d**[26] were prepared according to the reported procedures. Zinc borohydride was prepared as follows: A solution of $ZnCl_2$ (2 g, 14.7 mmol) in dry diethyl ether (25 ml) was refluxed under nitrogen for 3 h. After cooling to room temperature, the solution was separated by decantation. This solution was added to a solution of $NaBH_4$ (1.31 g, 34.5 mmol) in ether (75 ml) and the solution was stirred under nitrogen for 18 h. The solution separated by decantation contains $Zn(BH_4)_2$ in the concentration of 0.36 M (1 M=1 mol dm^{-3}).

General Procedure for the Preparation of 2-Silyloxy-1,3-dienes 2a—e. Silylation of **1d** is described as a typical procedure. A mixture of **1d** (3.31 g, 23.6 mmol), Me_3SiCl (3.6 ml, 28.3 mmol), and DBU (4.59 ml, 30.7 mmol) in dry CH_2Cl_2 (10 ml) was refluxed for 2 h under nitrogen. After cooled to room temperature, the mixture was poured into hexane (450 ml). The colorless solid (DBU · HCl) precipitated was filtered off, the filtrate was quickly washed with ice water, and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue (5.93 g) was distilled under reduced pressure to give **2d** (4.63 g, 92%) as pale yellow liquid.

The other 2-silyloxy-1,3-dienes **2a**—**c** and **2e** were similarly prepared in the yields shown in Table 1.

(*E*)-1-Phenyl-3-(trimethylsilyloxy)-1,3-butadiene (2a): Prepared according to the reported method.[14]

(*E*)-5,5-Dimethyl-2-(trimethylsilyloxy)-1,3-hexadiene (2b): Pale yellow liquid; bp 108 °C/60 mmHg (1 mmHg=133.322 Pa) (bulb-to-bulb); IR (neat) 2950, 1600, 1460, 1310, 1260, 1030, and 900 cm^{-1}; ^{1}H NMR (C_6D_6) δ=0.19 (9H, s, $SiMe_3$), 0.99 (9H, s, *t*-Bu), 4.32, 4.35 (each 1H, each br s, H-1), 5.93 (1H, d, J_{3-4}=15.4 Hz, H-3), and 6.25 (1H, d, J_{4-3}=15.4 Hz, H-4); ^{13}C NMR (C_6D_6) δ=0.10 ($SiMe_3$), 29.59 (*t*-Bu), 32.79 (*t*-Bu), 94.55 (C-1), 123.50 (C-3), 142.30 (C-4), and 155.78 (C-2); MS *m/z* (rel intensity, %) 199 (M^++1, 10), 198 (M^+, 57), 183 (63), 155 (23), 141 (base peak), 93 (22), 75 (51), and 73 (80). HRMS Found: *m/z* 198.1440. Calcd for $C_{11}H_{22}OSi$: M, 198.1439.

(1*E*,3*Z*)-1-Phenyl-3-(trimethylsilyloxy)-1,3-pentadiene (2c): Pale yellow liquid; bp 140 °C/27 mmHg (bulb-to-bulb); IR (neat) 2950, 1620, 1400, 1370, 1320, 1240, 1190, 1020, 930, 820, 740, and 680 cm^{-1}; ^{1}H NMR (C_6D_6) δ=0.23 (9H, s, $SiMe_3$), 1.67 (3H, d, J_{5-4}=7.0 Hz, H-5), 4.89 (1H, q, J_{4-5}=7.0 Hz, H-4), 6.58 (1H, d, J_{2-1}=15.8 Hz, H-2), 6.84 (1H, d, J_{1-2}=15.8 Hz, H-1), and 7.01—7.30 (5H, m, Ph); ^{13}C NMR (C_6D_6) δ=0.73 ($SiMe_3$), 12.15 (C-5), 110.98 (C-4), 126.84, 127.12, 127.47, 127.92, 128.88, 137.65 (C-2, C-3, and Ph), and 150.45 (C-1); MS *m/z* (rel intensity, %) 233 (M^++1, 21), 232 (M^+, base peak), 231 (28), 217 (46), 203 (39), 75 (36), and 73 (68). Found: C, 72.47; H, 8.33%. Calcd for $C_{14}H_{20}OSi$: C, 72.34; H, 8.68%.

(2*Z*,4*E*)-6,6-Dimethyl-3-(trimethylsilyloxy)-2,4-heptadiene (2d): Pale yellow liquid; bp 150 °C/40 mmHg (bulb-to-bulb); IR (neat) 2950, 1620, 1450, 1330, 1240, 1200, 1030, 840, and 750 cm^{-1}; ^{1}H NMR (C_6D_6) δ=0.23 (9H, s, $SiMe_3$), 1.01 (9H, s, *t*-Bu), 1.65 (3H, d, J_{1-2}=7.0 Hz, H-1), 4.75 (1H, q, J_{2-1}=7.0 Hz, H-2), 5.89 (1H, d, J_{4-5}=15.8 Hz, H-4), and 5.98 (1H, d, J_{5-4}=15.8 Hz, H-5); NOE: H-2/H-4; ^{13}C NMR (C_6D_6) δ=0.85 ($SiMe_3$), 11.84 (C-1), 29.79 (*t*-Bu), 32.80 (*t*-Bu), 107.70 (C-2), 124.34 (C-4), 139.59 (C-5), and 150.26 (C-3); MS *m/z* (rel

intensity, %) 213 (M^++1, 20), 212 (M^+, base peak), 197 (53), 183 (39), 169 (21), 155 (51), 107 (32), 75 (34), and 73 (91). HRMS Found: m/z 212.1597. Calcd for $C_{12}H_{24}OSi$: M, 212.1595.

(2*Z*,4*E*)-3-(Trimethylsilyloxy)-2,4-hexadiene (2e); Pale yellow liquid; bp 100 °C/18 mmHg; IR (neat) 2950, 1620, 1430, 1360, 1330, 1250, 1200, 1030, 910, 830, and 740 cm^{-1}; ^1H NMR (C_6D_6) δ=0.19 (9H, s, $SiMe_3$), 1.61—1.64 (6H, m, H-1 and H-6), 4.69 (1H, q, J_{2-1}=7.0 Hz, H-2), and 5.84—5.88 (2H, m, H-4 and H-5); ^{13}C NMR (C_6D_6) δ=0.75 ($SiMe_3$), 11.76 (C-1), 17.62 (C-6), 107.14 (C-2), 123.08 (C-4), 130.81 (C-5), and 150.07 (C-3); MS m/z (rel intensity, %) 171 (M^++1, 11), 170 (M^+, 65), 155 (base peak), 141 (57), 75 (98), and 73 (93); HRMS Found: m/z 170.1132. Calcd for $C_9H_{18}OSi$: M, 170.1126.

Generation of 1,3-Dien-2-olates 3a—e and 3d'. A) From 2a—e and Butyllithium: As a typical procedure the generation of **3d** from **2d** is described: To a solution of **2d** (0.212 g, 1 mmol) in dry THF (2 ml) was added, at −78 °C under nitrogen, *n*-BuLi (1.6 M in hexane, 0.63 ml, 1 mmol). The mixture was stirred at −78 °C for 30 min and the stirring was continued for additional 30 min at room temperature to provide the THF solution of **3d**. We refer to the solution thus prepared as the standard solution of **3d**, and also the standard solutions of **3a**—**c** and **3e** were prepared by similar methods.

B) From 1d and LDA: To a solution of diisopropylamine (0.168 ml, 0.121 g, 1.2 mmol) in THF (3 ml) was added, at −78 °C under nitrogen, *n*-BuLi (1.6 M in hexane, 0.75 ml, 1.1 mmol). After stirring for 20 min, **1d** (0.14 g, 1 mmol) in THF (5 ml) was slowly added (in a period of 25 min by the aid of a Micro Feeder) and the stirring was continued at −78 °C for additional 15 min to give a solution of **3d** and **3d'** (67 : 33).

C) From 1d and LHMDS: To a solution of 1,1,1,3,3,3-hexamethyldisilazane (0.232 ml, 0.177 g, 1.1 mmol) in THF (3 ml) was added, at −78 °C under nitrogen, *n*-BuLi (0.66 ml, 1.05 mmol). After stirring for 20 min, **1d** (0.14 g, 1 mmol) in THF (5 ml) was slowly added (in a period of 25 min by the aid of a Micro Feeder) and the stirring was continued at −78 °C for additional 15 min to give a solution of **3d** and **3d'** (88 : 12).

D) From 1d and LTMP: To a solution of 2,2,6,6-tetramethylpiperidine (0.186 ml, 0.155 g, 1.1 mmol) in THF (3 ml) was added, at −78 °C under nitrogen, *n*-BuLi (0.66 ml, 1.05 mmol). After stirring for 20 min, **1d** (0.14 g, 1 mmol) in THF (5 ml) was slowly added (in a period of 25 min by the aid of a Micro Feeder) and the stirring was continued at −78 °C for additional 15 min to give a solution of **3d** and **3d'** (67 : 33).

Generation of 3d Followed by Acetylation Leading (2*Z*,4*E*)-3-Acetoxy-6,6-dimethyl-2,4-heptadiene (4). To a solution of **2d** (0.106 g, 0.5 mmol) in THF (I ml) was added, at −78 °C under nitrogen, *n*-BuLi (1.6 M in hexane, 0.32 ml, 0.5 mmol). After 30 min at −78 °C, the stirring was continued for additional 30 min at room temperature, and then cooled to −78 °C. Acetic anhydride (0.057 ml, 0.6 mmol) was added and the mixture was stirred for 40 min. The resulting mixture was poured into saturated aqueous NH_4Cl and extracted with CH_2Cl_2 (15 ml×3). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue (0.091 g) was chromatographed on silica gel using hexane–EtOAc (15 : 1) to give **4** (0.077 g, 85%). Pale yellow liquid; IR (neat) 2950, 1750, 1430, 1360, 1190, 1010, 950, 900, and 770 cm^{-1}; ^1H NMR (C_6D_6) δ=0.97 (9H, s, *t*-Bu), 1.49 (3H, d, J_{1-2}=7.0 Hz, H-1), 1.80 (3H, s, OCOMe), 5.07 (1H, q, J_{2-1}=7.0 Hz, H-2), 5.79, and 5.89 (each 1H, each d, J_{4-5}=15.8 Hz, H-4 and H-5); ^{13}C NMR (C_6D_6) δ=11.40 (C-1), 19.91 (OCOMe), 29.60 (C-7), 32.86 (*t*-Bu), 114.57 (C-2), 121.13 (C-4), 139.55 (C-5), 147.53 (C-3), and 166.89 (OCOMe); MS m/z (rel intensity, %) 183 (M^++1, 4), 182 (M^+, 31), 140 (89), 125 (31), 111 (base peak), and 43 (33). HRMS Found: m/z 182.1308. Calcd for $C_{11}H_{18}O_2$: M, 182.1306.

General Procedure for the Reactions of Lithium 1,3-Dien-2-olates 3 with α,β-Unsaturated Esters Leading to 5a—c. The reaction of **3d** with methyl crotonate is described as a typical example: To the standard solution of **3d** generated from **2d** (0.425 g, 2 mmol) was added, at −78 °C under nitrogen, methyl crotonate (0.2 g, 2 mmol) in THF (1 ml). After stirring at −78 °C for 1.5 h and then at room temperature for 26 h, the mixture was poured into saturated aqueous NH_4Cl and then extracted with CH_2Cl_2 (20 ml×3). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue (0.546 g) was chromatographed on silica gel with hexane–EtOAc (30 : 1, v/v) to give **5a** (0.235 g, 49%).

***c*-5-*t*-Butyl-*t*-4-(methoxycarbonyl)-*r*-2,*c*-3-dimethylcyclohexanone (5a):** Pale yellow liquid; IR (neat) 2950, 1730, 1705, 1440, 1360, 1300, 1160, and 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.89 (3H, d, J_{Me-3}=7.3 Hz, 3-Me), 0.90 (9H, s, *t*-Bu), 0.96 (3H, d, J_{Me-2}=7.0 Hz, 2-Me), 1.89 (1H, ddd, J_{5-4}=3.8, J_{5-6eq}=4.0, and J_{5-6ax}=14.3 Hz, H-5), 2.26—2.39 (2H, m, H-3 and H-6_{eq}), 2.81 (1H, dd, J_{4-3}=3.3 and J_{4-5}=3.8 Hz, H-4), 2.99 (1H, dd, J_{gem}=13.2 and J_{6ax-5}=14.3 Hz, H-6_{ax}), 3.33 (1H, dq, J_{2-Me}=J_{2-3}=7.0 Hz, H-2), and 3.72 (3H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ=11.63 (3-Me), 15.55 (2-Me), 27.96 (*t*-Bu), 33.00 (C-3), 39.65, 39.81 (C-5 and *t*-Bu), 43.45 (C-6), 45.76, 46.68 (C-2 and C-4), 51.56 (COOMe), 175.42 (COOMe), and 213.63 (C-1); MS m/z (rel intensity, %) 241 (M^++1, 8), 240 (M^+, 31), 184 (21), 183 (base peak), 127 (44), and 126 (15). Found: C, 69.94; H, 10.00%. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07%.

***r*-3-*t*-Butyl-*c*-4-(methoxycarbonyl)-*t*-5-methylcyclohexanone (5b):** Similar procedure using **2b** (0.397 g, 2 mmol), *n*-BuLi (2 mmol), and methyl crotonate (0.2 g, 2 mmol) under stirring at −78 °C for 2.3 h and then at room temperature for 1.5 h followed by silica-gel column chromatography with hexane–EtOAc (6 : 1, v/v) gave **5b** (0.392 g, 87%): Pale yellow liquid; IR (neat) 2950, 2900, 1700, and 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.91 (9H, s, *t*-Bu), 1.06 (3H, d, J_{Me-5}=7.3 Hz, 5-Me), 1.93 (1H, dt, J_{3-2eq}=J_{3-4}=3.8 and J_{3-2ax}=13.9 Hz, H-3), 2.03 (1H, br dd, J_{6eq-5}=2.2 and J_{gem}=14.3 Hz, H-6_{eq}), 2.27 (1H, br dd, J_{2eq-3}=3.8 and J_{gem}=13.9 Hz, H-2_{eq}), 2.43 (1H, dtq, J_{5-6eq}=J_{5-4}=2.2 Hz, J_{5-6ax}=6.6, and J_{5-Me}=7.3 Hz, H-5), 2.77 (1H, br dd, J_{4-5}=2.2 and J_{4-3}=3.8 Hz, H-4), 2.93 (1H, t, J_{gem}=J_{2ax-3}=13.9 Hz, H-2_{ax}), 3.04 (1H, dd, J_{6ax-5}=6.6 and J_{gem}=14.3 Hz, H-6_{ax}), and 3.70 (3H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ=20.65 (5-Me), 27.83 (*t*-Bu), 32.92 (C-5), 33.30 (C-3), 39.39 (*t*-Bu), 43.84, 44.71, 44.88 (C-2, C-4, and C-6), 51.40 (COOMe), 175.19 (COOMe), and 211.27 (C-1); MS m/z (rel intensity, %) 227 (M^++1, 8), 226 (M^+, 15), 170 (23), 169 (base peak), 127 (10), and 110 (23). HRMS Found: m/z 226. 1575. Calcd for $C_{13}H_{22}O_3$: M, 226.1568.

***r*-3-*t*-Butyl-*c*-4-(methoxycarbonyl)-*t*-4-methylcyclohexanone (5c):** Similar procedure using **2b** (0.397 g, 2 mmol), *n*-BuLi (2 mmol), and methyl methacrylate (0.2 g, 2 mmol) under stirring at −78 °C for 2.5 h and then at room temperature for 22 h followed by silica-gel column chromatography with hexane–EtOAc (7 : 1, v/v) gave **5c** (0.045 g, 20%): Pale yellow liquid; IR (neat) 2950, 1720, 1450, 1200, and 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.95 (9H, s, *t*-Bu), 1.45 (3H, s, 4-Me),

1.74—1.86 (2H, m, H-3_{eq} and H-5), 2.16—2.88 (5H, m, H-2, H-6, and H-3_{ax}), and 3.72 (3H, s, COOMe); ^{13}C NMR ($CDCl_3$) δ=27.33 (4-Me), 29.62 (*t*-Bu), 35.10 (C-5), 35.85 (C-3), 36.92 (*t*-Bu), 40.72 (C-2), 44.28 (C-6), 51.62 (COOMe), 53.46 (C-4), 176.83 (COOMe), and 212.72 (C-1); MS *m/z* (rel intensity, %) 227 (M^++1, 5), 226 (M^+, 1), 171 (17), 170 (57), 169 (47), 138 (15), 111 (40), and 110 (base peak). Found: C, 69.14; H, 9.65%. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80%.

Reaction of 3d with Methyl Crotonate in the Presence of $ZnCl_2$ Leading to Methyl (3*RS*,4*RS*,6*E*)-3,4,8,8-Tetramethyl-5-oxo-6-nonenoate (6). To a solution of **2d** (0.425 g, 2 mmol) in THF (1 ml) was added, at −78 °C under nitrogen, *n*-BuLi (1.6 M in hexane, 1.25 ml, 2 mmol). After stirring at −78 °C for 20 min and at room temperature for additional 30 min, the mixture was cooled down to −20 to −30 °C and a solution of $ZnCl_2$ (0.273 g, 2 mmol) in THF (1.5 ml) was added. After 20 min, the mixture was cooled down to −78 °C and methyl crotonate (0.2 g, 2 mmol) in THF (1 ml) was added. Stirring was continued at −78 °C for 20 h and at room temperature for 52 h. The mixture was poured into saturated aqueous NH_4Cl and extracted with CH_2Cl_2 (15 ml×3). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue (0.366 g) was chromatographed on silica gel using hexane–EtOAc (15 : 1) to give **6** (0.087 g, 18%): Pale yellow liquid; IR (neat) 2950, 1740, 1630, and 1460 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.97 (3H, d, J_{Me-3}=6.2 Hz, 3-Me), 1.07 (3H, d, J_{Me-4}=7.0 Hz, 4-Me), 1.09 (9H, s, *t*-Bu), 2.12 (1H, dd, J_{2-3}=8.8 and J_{gem}=14.7 Hz, one of H-2), 2.29—2.46 (2H, m, H-3 and the other of H-2), 2.74 (1H, quint, J_{4-3}=J_{4-Me}=7.0 Hz, H-4), 3.67 (3H, s, COOMe), 6.08 (1H, d, J_{6-7}=16.1 Hz, H-6), and 6.87 (1H, d, J_{7-6}=16.1 Hz, H-7); ^{13}C NMR ($CDCl_3$) δ=13.36 (3-Me), 18.33 (4-Me), 28.74 (*t*-Bu), 29.62 (C-3), 32.41 (C-2), 33.79 (*t*-Bu), 37.75 (C-4), 51.46 (COOMe), 124.32 (C-6), 157.42 (C-7), 173.36 (COOMe), and 203.52 (C-5); MS *m/z* (rel intensity, %) 241 (M^++1, 3), 240 (M^+, 5), 140 (17), and 111 (base peak). HRMS Found *m/z* 240.1723. Calcd for $C_{14}H_{24}O_3$: M, 240.1724.

Reaction of 3d with Methyl (*E*)-4-Bromo-2-butenoate Leading to Methyl (1*RS*,2*SR*)-2-[(1*RS*,3*E*)-1,5,5-Trimethyl-2-oxo-3-hexenyl]-1-cyclopropanecarboxylate (7). To a solution of **2d** (0.212 g, 1 mmol) in THF (1 ml) was added, at −78 °C under nitrogen, *n*-BuLi (1.6 M in hexane, 0.63 ml, 1 mmol). After 20 min at −78 °C, stirring was continued for additional 20 min at room temperature, and then cooled to −78 °C. To this mixture was added a solution of methyl (*E*)-4-bromo-2-butenoate (0.179 g, 1 mmol) in THF (1 ml). The mixture was stirred at −78 °C for 17 h, poured into saturated aqueous NH_4Cl, and then extracted with CH_2Cl_2 (15 ml×3). The combined extracts were dried over $MgSO_4$ and evaporated in vacuo. The residue (0.205 g) was chromatographed on silica gel with hexane–EtOAc (15 : 1) to give **7** (0.118 g, 50%): Pale yellow liquid; IR (neat) 2950, 1730, 1700, 1660, 1620, 1450, 1210, 1170, 990, and 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.86 (1H, ddd, J_{3-1}=4.4, J_{3-2}=6.2, and J_{gem}=8.4 Hz, one of H-3), 1.10 (9H, s, *t*-Bu), 1.13—1.28 (1H, m, the other of H-3), 1.20 (3H, d $J_{Me-1'}$=7.0 Hz, Me), 1.49 (1H, dt, J_{1-2}=J_{1-3}=4.4, and J_{1-3}=8.4 Hz, H-1), 1.60 (1H, dddd, J_{2-1}=4.4, J_{2-3}=6.2, $J_{2-1'}$=9.2, and J_{2-3}=10.6 Hz, H-2), 2.20 (1H, dq, $J_{1'-Me}$=7.0 and $J_{1'-2}$=9.2 Hz, H-1′), 3.70 (3H, s, COOMe), 6.12 (1H, d, $J_{3'-4'}$=15.8 Hz, H-3′), and 6.88 (1H, d, $J_{4'-3'}$=15.8 Hz, H-4′); ^{13}C NMR ($CDCl_3$) δ=14.85 (Me), 16.27 (C-3), 18.98 (C-2), 25.20 (C-1), 28.70 (*t*-Bu), 33.87 (*t*-Bu), 47.62 (C-1′), 51.78 (COOMe), 123.18 (C-3′), 157.89 (C-4′), 174.23 (COOMe), and 201.91 (C-2′); MS *m/z* (rel intensity, %) 239 (M^++1, 2), 238 (M^+, 12), and 111 (base peak). HRMS Found: *m/z* 238.1571. Calcd for $C_{14}H_{22}O_3$: M, 238.1568.

Reaction of 3d with 1-Phenyl-2-buten-1-one Leading to 8 and 8′. A) To the standard solution of **3d** prepared from **2d** (0.106 g, 0.5 mmol) was added under nitrogen at −78 °C a solution of 1-phenyl-2-buten-1-one (0.073 g, 0.5 mmol, *Z* : *E*=10 : 90). After stirring at −78 °C for 1 h, the mixture was poured into saturated aqueous NH_4Cl and extracted with CH_2Cl_2 (10 ml×3). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue (0.16 g) was chromatographed on silica gel with hexane–EtOAc (10 : 1, v/v) to give an inseparable mixture of **8** and **8′** (0.104 g, 73%, **8** : **8′**=87 : 13 by ^{1}H NMR).

B) To a solution of **2d** (0.212 g, 1 mmol) in dry THF/HMPA (4 ml/0.5 ml) was added under nitrogen at −78 °C *n*-BuLi (1.6 M in hexane, 0.63 ml, 1 mmol). After 20 min, a solution of 1-phenyl-2-buten-1-one (0.146 g, 1 mmol, *Z* : *E*=9 : 91) was added, and the reaction was continued for 30 min. Similar workup and chromatographic purification gave **8** and **8′** (0.239 g, 84%, **8** : **8′**=95 : 5 by ^{1}H NMR).

C) To the standard solution of **3d** prepared from **2d** (0.212 g, 1 mmol) was added under nitrogen 18-Crown-6 (0.264 g, 1 mmol) in dry THF (2 ml). After 15 min, a solution of 1-phenyl-2-buten-1-one (0.146 g, 1 mmol, *Z* : *E*=9 : 91) was added, and the reaction was continued for 2.5 h. Similar workup and chromatographic purification gave **8** and **8′** (0.233 g, 81%, **8** : **8′**=95 : 5 by ^{1}H NMR).

3,4,8,8-Tetramethyl-1-phenyl-6-nonene-1,5-dione (8+8′): Isomer 8: Pale yellow liquid; IR (neat) 2950, 1660, 1610, 1450, 1360, 1260, 1200, and 980 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.01 (3H, d, J_{Me-3}=6.6 Hz, 3-Me), 1.07 (9H, s, *t*-Bu), 1.13 (3H, d, J_{Me-4}=7.0 Hz, 4-Me), 2.51—2.66 (1H, m, H-3), 2.71 (1H, dd, J_{2-3}=9.3 and J_{gem}=15.8 Hz, one of H-2), 2.86 (1H, dq, J_{4-3}=5.1 and J_{4-Me}=7.0 Hz, H-4), 3.08 (1H, dd, J_{2-3}=3.3 and J_{gem}=15.8 Hz, the other of H-2), 6.11 (1H, d, J_{6-7}=16.1 Hz, H-6), 6.89 (1H, d, J_{7-6}=16.1 Hz, H-7), 7.41—7.58, and 7.91—8.00 (3H and 2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=12.60 (3-Me), 18.40 (4-Me), 28.71 (*t*-Bu), 31.46 (C-3), 33.78 (*t*-Bu), 41.55 (C-4), 48.67 (C-2), 124.23 (C-6), 128.10, 128.56, 132.98, 137.14 (each Ph), 157.40 (C-7), 199.76 (C-5), and 203.69 (C-1); MS *m/z* (rel intensity, %) 287 (M^++1, 8), 286 (M^+, 36), 230 (12), 167 (40), 140 (34), 111 (base peak), and 105 (25). Found: C, 79.46; H, 9.08%. Calcd for $C_{19}H_{26}O_2$: C, 79.67; H, 9.16%.

Isomer 8′: Its formation was deduced on the basis of ^{1}H and ^{13}C NMR spectra of the crude reaction mixture because **8′** could not be separated from the mixture with **8**: Partial ^{1}H NMR ($CDCl_3$) δ=0.92 (3H, d, J_{Me-3}=6.6 Hz, 3-Me), 1.07 (3H, d, J_{Me-4}=7.0 Hz, 4-Me), 1.09 (9H, s, *t*-Bu), 6.13 (1H, d, J_{trans}=15.8 Hz, H-6), 6.94 (1H, d, J_{trans}=15.8 Hz, H-7), 7.41—7.60, and 7.92—8.00 (5H, m, Ph). Other signals are overlapping with those of **8**. Partial ^{13}C NMR ($CDCl_3$) δ=12.08 (3-Me), 16.08 (4-Me), 28.71 (C-9), 31.42 (C-3), 33.79 (C-8), 43.67 (C-4), 47.86 (C-2), 124.14 (C-6), 128.16, 128.62, 133.07, 137.06 (each Ph), 157.56 (C-7), 199.69 (C-5), and 203.90 (C-1).

Reaction of 3d with 1-Phenyl-2-buten-1-one Leading to 9+9′+9″. To the standard solution of **3d** prepared from **2d** (0.106 g, 0.5 mmol) was added, under nitrogen at −78 °C, 1-phenyl-2-buten-1-one (0.074 g, 0.5 mmol, *Z* : *E*=10 : 90 by ^{1}H NMR) in THF (1 ml). After stirring at −78 °C for 30 min and then at room temperature for 42 h, the mixture was poured into saturated NH_4Cl and extracted with CH_2Cl_2 (10 ml×3). The combined extracts were dried ($MgSO_4$) and

evaporated in vacuo. The residue (0.137 g) was chromatographed on silica gel with hexane–EtOAc (20 : 1, v/v) to give a mixture of **9**, **9′**, and **9″** (0.101 g, 71%, 62 : 16 : 22 by GLC), which were separated from each other by careful chromatographic operation.

***t*-4-Benzoyl-*t*-5-*t*-butyl-*r*-2,*c*-3-dimethylcyclohexanone (9):** Pale yellow solid; mp 65—68 °C; IR (KBr) 2900, 1660, 1200, and 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.87 (9H, s, *t*-Bu), 0.93 (3H, d, J_{Me-2}=6.6 Hz, 2-Me), 1.05 (3H, d, J_{Me-3}=7.3 Hz, 3-Me), 2.06 (1H, dt, J_{5-6eq}=J_{5-4}=4.0 and J_{5-6ax}=13.9 Hz, H-5), 2.27 (1H, ddq, J_{3-4}=1.5, J_{3-2}=6.2, and J_{3-Me}=7.3 Hz, H-3), 2.40 (1H, ddd, J_{6eq-4}=1.1, J_{6eq-5}=4.0, and J_{gem}=13.9 Hz, H-6_{eq}), 3.07 (1H, dq, J_{2-3}=6.2 and J_{2-Me}=6.6 Hz, H-2), 3.43 (1H, t, J_{6ax-5}=J_{gem}=13.9 Hz, H-6_{ax}), 3.86 (1H, ddd, J_{4-6eq}=1.1, J_{4-3}=1.5, and J_{4-5}=4.0 Hz, H-4), 7.48—7.65, and 7.79—8.02 (3H and 2H, m, Ph); NOE: H-2/H-3, H-2/H-6_{ax}, 2-Me/H-5, and 3-Me/H-5; ^{13}C NMR ($CDCl_3$) δ=11.68 (2-Me), 15.69 (3-Me), 28.94 (*t*-Bu), 33.36 (*t*-Bu), 39.34, 40.68 (C-3 and C-5), 42.94 (C-6), 46.72, 46.81 (C-2 and C-4), 128.12, 128.98, 133.24, 137.22 (each Ph), 203.28 (COPh), and 214.15 (C-1); MS *m/z* (rel intensity, %) 286 (M^+, 26), 230 (35), 229 (46), 174 (71), 173 (56), 111 (32), 105 (base peak), 83 (24), and 77 (34). Found: C, 79.37; H, 8.96%. Calcd for $C_{19}H_{26}O_2$: C, 79.67; H, 9.16%.

***t*-4-Benzoyl-*t*-5-*t*-butyl-*r*-2,*t*-3-dimethylcyclohexanone (9′):** Pale yellow solid; mp 108—111 °C; IR (KBr) 2900, 1650, 1440, 1200, and 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.82 (9H, s, *t*-Bu), 0.97 (3H, d, J_{Me-2}=7.0 Hz, 2-Me), 1.03 (3H, d, J_{Me-3}=7.0 Hz, 3-Me), 1.81—1.96 (2H, m, H-3 and H-5), 2.43 (1H, ddd, J_{6eq-4}=1.1, J_{6eq-5}=3.7, and J_{gem}=13.4 Hz, H-6_{eq}), 2.87 (1H, dq, J_{2-Me}=7.0 and J_{2-3}=12.4 Hz, H-2), 3.30 (1H, t, J_{6ax-5}=J_{gem}=13.4 Hz, H-6_{ax}), 4.16 (1H, br t, J_{4-3}=J_{4-5}=3.7 Hz, H-4), 7.48—7.64, and 8.04—8.08 (3H and 2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=11.71 (2-Me), 18.23 (3-Me), 28.51 (*t*-Bu), 33.74 (*t*-Bu), 39.55, 43.57 (C-3 and C-5), 44.66 (C-6), 45.59 (C-2), 53.35 (C-4), 128.49, 128.89, 133.20, 139.49 (each Ph), 204.53 (COPh), and 213.87 (C-1); MS *m/z* (rel intensity, %) 286 (M^+, 23), 230 (37), 229 (31), 174 (63), 173 (52), 167 (25), 140 (14), 111 (94), 105 (base peak), 83 (28), and 77 (42). HRMS Found: *m/z* 286.1932. Calcd for $C_{19}H_{26}O_2$: M, 286.1931.

***c*-4-Benzoyl-*c*-5-*t*-butyl-*r*-2,*c*-3-dimethylcyclohexanone (9″):** Pale yellow liquid; IR (neat) 3400, 2950, 1660, 1590, 1570, 1440, 1360, 1280, 1200, 1060, 990, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.86 (9H, s, *t*-Bu), 1.08 (3H, d, J_{Me-2}=6.6 Hz, 2-Me), 1.33 (3H, d, J_{Me-3}=7.0 Hz, 3-Me), 1.64 (1H, ddq, J_{3-4}=1.8, J_{3-Me}=7.0, and J_{3-2}=8.4 Hz, H-3), 2.15 (1H, dq, J_{2-Me}=6.6 and J_{2-3}=8.4 Hz, H-2), 2.26—2.88 (3H, m, H-5 and H-6), 3.68 (1H, br s, H-4), 7.45—7.60, and 7.91—7.94 (3H and 2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=13.59 (2-Me), 22.02 (3-Me), 28.45 (*t*-Bu), 33.04 (*t*-Bu), 38.21,40.24 (C-3 and C-5), 44.48, 45.34 (C-2 and C-6), 47.44 (C-4), 128.17, 128.88, 133.11, 137.50 (each Ph), 204.23 (COPh), and 212.91 (1-C); MS *m/z* (rel intensity, %) 287 (M^++1, 3), 286 (M^+, 8), 259 (28), 230 (73), 174 (base peak), 173 (31), and 105 (24). HRMS Found: *m/z* 286.1934. Calcd for $C_{19}H_{26}O_2$: M, 286.1931.

2,4-Dibenzoyl-3,5,6-trimethyl-1-[(*E*)-3,3-dimethyl-1-butenyl]cyclohexanol (10). To the standard solution of **3d** prepared from **2d** (0.182 g, 0.86 mmol) were added, under nitrogen at −78 °C, 1-phenyl-2-buten-1-one (0.125 g, 0.86 mmol, *Z* : *E*=1 : 99 by ^1H NMR) in THF (1 ml) and HMPA (0.5 ml) in THF (1 ml). After stirring at −78 °C for 1 h, the mixture was poured into saturated NH_4Cl and extracted with CH_2Cl_2 (10 ml×3). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue (0.675 g) was triturated with hexane to give **10** (0.104 g, 28%). The filtrate was evaporated in vacuo and the residue was chromatographed on silica gel with hexane–EtOAc (15 : 1, v/v) to give **8** and **8′** (0.159 g, 65%, **8** : **8′**=83 : 17 by ^1H NMR). **10**: Colorless solid; mp 218—220 °C (decomp); IR (KBr) 3400, 2850, 1200, and 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.63 (9H, s, *t*-Bu), 0.83 (3H, d, J_{Me-3}=6.2 Hz, 3-Me), 0.92 (3H, d, J_{Me-6}=7.0 Hz, 6-Me), 0.97 (3H, d, J_{Me-5}=7.3 Hz, 5-Me), 1.90 (1H, dq, J_{6-5}=4.8 and J_{6-Me}=7.0 Hz, H-6), 2.17 (1H, ddq, J_{5-4}=4.4, J_{5-6}=4.8, and J_{5-Me}=7.3 Hz, H-5), 2.98 (1H, ddq, J_{3-Me}=6.2, J_{3-4}=11.0, and J_{3-2}=11.4 Hz, H-3), 3.53 (1H, dd, J_{4-5}=4.4 and J_{4-3}=11.0 Hz, H-4), 3.53 (1H, d, J_{2-3}=11.4 Hz, H-2), 4.01 (1H, br s, OH), 5.04, 5.48 (each 1H, each d, J_{trans}=15.8 Hz, =CH), 7.43—7.61, and 7.92—8.00 (3H and 2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=10.87, 13.42, 18.79 (3-, 5-, and 6-Me), 27.79 (C-5), 29.17 (*t*-Bu), 32.21 (*t*-Bu), 36.57 (C-6), 42.94 (C-3), 56.70,57.71 (C-2 and C-4), 75.20 (C-1), 128.06, 128.49, 128.61, 128.72, 129.95, 132.88, 133.55, 137.20, 138.79, 140.77 (=CH and Ph), 201.00, and 207.05 (2- and 4-COPh); MS *m/z* (rel intensity, %) 432 (M^+, 1), 414 (10), 294 (16), 268 (20), 267 (base peak), 266 (30), 147 (28), and 140 (50). Found: C, 80.74; H, 8.26%. Calcd for $C_{29}H_{36}O_3$: C, 80.51; H, 8.39%.

Reaction of 3d with (*E*)-3-Penten-2-one Leading ot 11a and 12. To the standard solution of **3d** prepared from **2d** (0.212 g, 1 mmol) was added under nitrogen at −78 °C (*E*)-3-penten-2-one (0.084 g, 1 mmol) in THF (1 ml). After stirred at −78 °C for 1 h and then at room temperature for 20 h, the mixture was poured into saturated NH_4Cl and extracted with CH_2Cl_2 (15 ml×3). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue (0.197 g) was chromatographed on silica gel with hexane–EtOAc (15 : 1, v/v) to give **12** (0.101 g, 49%) and then **11a** (0.012 g, 5%).

***t*-4-Acetyl-*t*-5-butyl-*r*-2,*c*-3-dimethylcyclohexanone (11a):** This product could not be separated from the mixture with **12** because of the low yield. Its partial ^1H NMR spectrum was abstracted ($CDCl_3$) δ=0.91 (9H, s, *t*-Bu), 0.93 (3H, d, J_{Me-3}=7.3 Hz, 3-Me), 0.94 (3H, d, J_{Me-2}=6.2 Hz, 2-Me), 1.83 (1H, dt, J_{5-4}=J_{5-6eq}=3.8 and J_{5-6ax}=14.3 Hz, H-5), 2.18—2.23 (1H, m, H-3), 2.30 (1H, br dd, J_{6eq-5}=3.8 and J_{gem}=13.8 Hz, H-6_{eq}), 2.35 (3H, s, COMe), 2.95 (1H, quint, J_{2-Me}=J_{2-3}=6.2 Hz, H-2), 3.00 (1H, dd, J_{4-3}=1.8 and J_{4-5}=3.8 Hz, H-4), and 3.17 (1H, dd, J_{gem}=13.8 and J_{6ax-5}=14.3 Hz, H-6_{ax}).

***cis*-4,5-Dimethyl-3-[(*E*)-3,3-dimethyl-1-butenyl]-2-cyclohexen-1-one (12):** Pale yellow liquid; IR (neat): 2950, 1660, 1640, 1590, 1460, 1300, 1250, 1190, and 980 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.06 (3H, d, J_{Me-4}=7.3 Hz, 4-Me), 1.07 (3H, d, J_{Me-5}=6.2 Hz, 5-Me), 1.10 (9H, s, *t*-Bu), 2.23—2.35 (3H, m, H-5 and H-6), 2.67 (1H, dq, J_{4-5}=3.7 and J_{4-Me}=7.3 Hz, H-4), 5.83 (1H, s, H-2), 6.00, and 6.25 (each 1H, each d, J_{trans}=16.1 Hz, =CH); ^{13}C NMR ($CDCl_3$) δ=12.43 (5-Me), 18.57 (4-Me), 29.19 (*t*-Bu), 32.14 (C-6), 40.49 (C-4), 125.04 (C-1′), 125.44 (C-2), 149.15 (C-3), 164.33 (C-2′), and 200.41 (C-1); MS *m/z* (rel intensity, %) 207 (M^++1, 15), 206 (M^+, 79), 191 (base peak), 150 (24), 135 (20), 121 (55), and 107 (21). HRMS Found: *m/z* 206.1673. Calcd for $C_{14}H_{22}O$: M, 206.1670.

***c*-4-Acetyl-*r*-3-*t*-butyl-*t*-5-methylcyclohexanone (11b):** A similar procedue using the standard solution of **3b** prepared from **2b** (0.397 g, 2 mmol) and (*E*)-3-penten-2-one (0.168 g, 2 mmol) at room temperature for 4.5 h followed by chromatographic purification (silica gel, hexane–EtOAc (7 : 1, v/v)) gave **11b** (0.131 g, 31%): Pale yellow liquid; IR (neat) 2940, 1700, 1470, 1360, and 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.91

(9H, s, *t*-Bu), 0.95 (3H, d, J_{Me-5}=6.2 Hz, 5-Me), 1.87 (1H, ddd, J_{3-4}=3.7, J_{3-2eq}=4.0, and J_{3-2ax}=14.3 Hz, H-3), 2.04 (1H, br d, J_{gem}=13.9 Hz, H-2_{eq}), 2.34 (3H, s, COMe), 2.24—2.41 (2H, m, H-5 and H-6_{eq}), 2.76 (1H, br dd, J_{6ax-5}=6.2 and J_{gem}=14.5 Hz, H-6_{ax}), 2.94 (1H, br s, H-4), and 3.15 (1H, dd, J_{gem}=13.9 and J_{2ax-3}=14.3 Hz, H-2_{ax}); ^{13}C NMR ($CDCl_3$) δ=20.88 (5-Me), 28.39 (COMe), 28.71 (*t*-Bu), 32.15 (C-5), 39.06 (*t*-Bu), 40.07 (C-3), 43.38, 45.99 (C-2 and C-6), 50.78 (C-4), 212.32, and 212.72 (C-1 and COMe); MS *m/z* (rel intensity, %) 211 (M^++1, 8), 210 (M^+, 24), 210 (24), 195 (21), 154 (24), 153 (base peak), 139 (14), 112 (34), and 111 (25). Found: C, 73.97; H, 10.57%. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54%.

***c*-4-Acetyl-*r*-3,*t*-5-diphenylcyclohexanone (11c):** A similar procedure using the standard solution of **3a** prepared from **2a** (0.473 g, 2 mmol) and (*E*)-4-phenyl-3-buten-2-one (0.292 g, 2 mmol) at room temperature for 1.5 h followed by chromatographic purification (silica gel, hexane–EtOAc (5 : 1, v/v)) gave **11c** (0.183 g, 31%): Pale yellow liquid; IR (neat) 3250, 1770, 1560, 1520, 1430, and 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.63 (3H, s, COMe), 2.68 (1H, dd, J_{6eq-5}=5.1 and J_{gem}=15.4 Hz, H-6_{eq}), 2.73 (1H, dd, J_{2eq-3}=7.7 and J_{gem}=15.8 Hz, H-2_{eq}), 3.01 (1H, dd, J_{2ax-3}=6.2 and J_{gem}=15.8 Hz, H-2_{ax}), 3.20 (1H, dd, J_{6ax-5}=9.9 and J_{gem}=15.4 Hz, H-6_{ax}), 3.45 (1H, dd, J_{4-5}=5.5 and J_{4-3}=5.9 Hz, H-4), 3.55 (1H, ddd, J_{5-6eq}=5.1, J_{5-4}=5.5, and J_{5-6ax}=9.9 Hz, H-5), 3.62 (1H, ddd, J_{3-4}=5.9, J_{3-2ax}=6.2, and J_{3-2eq}=7.7 Hz, H-3), and 7.01—7.40 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=31.94 (COMe), 40.93, 41.12, 42.89, 44.22 (C-2, C-3, C-5, and C-6), 58.70 (C-4), 127.07, 127.22, 127.34, 127.66, 128.72, 128.97, 140.17, 143.09 (each Ph), 210.60, and 210.79 (C-1 and COMe); MS *m/z* (rel intensity, %) 293 (M^++1, 3), 292 (M^+, 6), 146 (85), 145 (55), 131 (base peak), 103 (84), and 86 (45). HRMS Found: *m/z* 292.1461. Calcd for $C_{20}H_{20}O_2$: M, 292.1462.

General Procedure for the Reactions of 3 with Dimethyl Alkylidenemalonates Leading to 13a—f. As a typical procedure the reaction of **3d** with dimethyl ethylidenemalonate is described: To the standard solution of **3d** prepared from **2d** (0.212 g, 1 mmol) was added under nitrogen at −78 °C dimethyl ethylidenemalonate (0.158 g, 1 mmol) in THF (0.5 ml). After stirring for 30 min at −78 °C, the mixture was poured into saturated aqueous NH_4Cl and extracted with CH_2Cl_2 (10 ml×3). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was chromatographed on silica gel with hexane–EtOAc (15 : 1, v/v) to give **13c** (0.25 g, 80%, *anti*/*syn*=60 : 40 by ^{1}H NMR). These isomers were separated and purified by careful chromatographic operation.

Dimethyl [(*E*)-1-Ethyl-2-methyl-3-oxo-5-phenyl-4-pentenylidene]malonate (13a): Two isomeric adducts were separated and purified through column chromatography on silica gel with hexane–EtOAc (15 : 1, v/v).

anti-**13a:** Pale yellow liquid; IR (neat) 2950, 1720, 1680, 1600, 1420, 1190, 1140, and 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.96 (3H, t, *J*=7.3 Hz, Me of Et), 1.17 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 1.50 (2H, dq, $J_{CH2-1'}$=5.9 and *J*=7.3 Hz, CH_2 of Et), 2.66 (1H, ddt, $J_{1'-CH2}$=$J_{1'-2}$=5.9 and $J_{1'-2'}$=7.0 Hz, H-1′), 3.10 (1H, dq, $J_{2'-Me}$=$J_{2'-1'}$=7.0 Hz, H-2′), 3.62 (1H, d, $J_{2-1'}$=5.9 Hz, H-2), 3.70, 3.75 (each 3H, each s, COOMe), 6.83 (1H, d, J_{trans}=15.8 Hz, H-4′), 7.37—7.65 (5H, m, Ph), and 7.60 (1H, d, J_{trans}=15.8 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ=12.74 (Et), 13.23 (2′-Me), 23.93 (Et), 41.99 (C-1′), 46.10 (C-2′), 52.34, 52.37, 52.48 (COOMe and C-2), 125.01 (C-4′), 128.40, 128.92, 130.49, 134.55, 142.72 (Ph and C-5′), 169.31, 169.54 (each COOMe), and 202.25 (C-3′); MS *m/z* (rel intensity, %) 333 (M^++1, 2), 332 (M^+, 8), 201 (21), 200 (43), 160 (76), and 131 (base peak); Found: C, 68.83; H, 7.41%. Calcd for $C_{19}H_{24}O_5$: C, 68.64; H, 7.28%.

syn-**13a:** Pale yellow liquid; IR (neat) 2950, 1720, 1690, 1430, 1200, and 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.84 (3H, t, *J*=7.3 Hz, Me of Et), 1.09 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 1.26—1.58 (2H, m, CH_2 of Et), 2.68—2.77 (1H, m, H-1′), 3.03 (1H, dq, $J_{2'-Me}$=4.4 and $J_{2'-1'}$=7.0 Hz, H-2′), 3.54 (1H, d, $J_{2-1'}$=8.1 Hz, H-2), 3.73, 3.78 (each 3H, each s, COOMe), 7.00 (1H, d, J_{trans}=15.8 Hz, H-4′), 7.39—7.64 (5H, m, Ph), and 7.69 (1H, d, J_{trans}=15.8 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ=10.99 (Et), 12.80 (2′-Me), 21.43 (Et), 41.01 (C-1′), 46.20 (C-2′), 52.48, 52.57 (each COOMe), 54.53 (C-2), 124.76 (C-4′), 128.48, 128.91, 130.42, 134.68, 142.86 (Ph and C-5′), 169.25, 169.41 (each COOMe), and 202.04 (C-3′); MS *m/z* (rel intensity, %) 333 (M^++1, 4), 332 (M^+, 21), 201 (21), 200 (26), 160 (84), and 131 (base peak). Found: C, 68.28; H, 7.42%. Calcd for $C_{19}H_{24}O_5$: C, 68.64; H, 7.28%.

Dimethyl [(*E*)-1,2,6,6-Tetramethyl-3-oxo-4-heptenylidene]malonate (13b): Obtained as a 52 : 48 inseparable mixture of *anti*-**13b** and *syn*-**13b** (by ^{1}H NMR) after column chromatography on silica gel using hexane–EtOAc (15 : 1, v/v). Colorless liquid; IR (neat) 2950, 1750, 1740, 1620, 1440, and 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$) *anti*-isomer δ=1.01 (3H, d, $J_{Me-1'}$=7.0 Hz, 1′-Me), 1.09 (9H, s, *t*-Bu), 1.12 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 2.50—2.63 (1H, m, H-1′), 2.85—2.97 (1H, m, H-2′), 3.59 (1H, d, $J_{2-1'}$=6.2 Hz, H-2), 3.75, 3.76 (each 3H, each s, COOMe), 6.06 (1H, d, J_{trans}=15.8 Hz, H-4′), and 6.86 (1H, d, J_{trans}=15.8 Hz, H-5′); *syn*-isomer δ=0.88 (3H, d, $J_{Me-1'}$=7.0 Hz, 1′-Me), 1.00 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 1.11 (9H, s, *t*-Bu), 2.68—2.81 (1H, m, H-1′), 2.85—2.97 (1H, m, H-2′), 3.41 (1H, d, $J_{2-1'}$=8.4 Hz, H-2), 3.73, 3.74 (each 3H, each s, COOMe), 6.12 (1H, d, J_{trans}=16.1 Hz, H-4′), and 6.94 (1H, d, J_{trans}=16.1 Hz, H-5′); ^{13}C NMR ($CDCl_3$) *anti*-isomer δ=12.44 (1′-Me), 14.86 (2′-Me), 28.73 (*t*-Bu), 33.84 (*t*-Bu), 36.11 (C-1′), 46.55 (C-2′), 52.24, 52.41 (each COOMe), 53.66 (C-2), 124.60 (C-4′), 157.68 (C-5′), 169.01, 169.08 (each COOMe), and 202.69 (C-3′); *syn*-isomer δ=11.00 (1′-Me), 15.36 (2′-Me), 28.73 (*t*-Bu), 33.84 (*t*-Bu), 34.34 (C-1′), 45.59 (C-2′), 52.34, 52.50 (each COOMe), 55.20 (C-2), 123.77 (C-4′), 157.89 (C-5′), 168.92, 169.45 (each COOMe), and 203.09 (C-3′); MS *m/z* (rel intensity, %) 299 (M^++1, 2), 298 (M^+, 8), 167 (21), 140 (30), and 111 (base peak). HRMS Found: *m/z* 298.1782. Calcd for $C_{16}H_{26}O_5$: M, 298.1779.

Dimethyl [(*E*)-1-Ethyl-2,6,6-trimethyl-3-oxo-4-heptenylidene]malonate (13c): *anti*-**13c:** Colorless liquid; IR (neat) 2980, 1755, 1735, 1620, and 1460 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.92 (3H, t, *J*=7.3 Hz, Me of Et), 1.07 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 1.10 (9H, s, *t*-Bu), 1.38—1.58 (2H, m, CH_2 of Et), 2.53—2.62 (1H, ddt, $J_{1'-2}$=5.9 and $J_{1'-2'}$=$J_{1'-CH_2}$=7.0 Hz, H-1′), 3.01 (1H, dq, $J_{2'-1'}$=7.0 and $J_{2'-Me}$=7.0 Hz, H-2′), 3.58 (1H, d, $J_{2-1'}$=5.9 Hz, H-2), 3.70, 3.74 (each 3H, each s, COOMe), 6.08 (1H, d, J_{trans}=16.1 Hz, H-4′), and 6.86 (1H, d, J_{trans}=16.1 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ=12.74 (Et), 13.33 (2′-Me), 23.86 (Et), 28.74 (*t*-Bu), 33.79 (*t*-Bu), 41.96 (C-1′), 45.54 (C-2′), 52.25, 52.30 (each COOMe), 52.44 (C-2), 124.11 (C-4′), 157.24 (C-5′), 169.35, 169.57 (each COOMe), and 203.06 (C-3′); MS *m/z* (rel intensity, %) 313 (M^++1, 2), 312 (M^+, 4), 180 (10), 140 (base peak), and 111 (89). Found: C, 65.55; H, 9.02%. Calcd for $C_{17}H_{28}O_5$: C, 65.34; H, 9.04%.

syn-**13c:** Colorless liquid; IR (neat) 2950, 1750, 1730, 1620, 1455, and 1430 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.83 (3H, t, *J*=7.3 Hz, Me of Et), 1.03 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 1.11 (9H, s,

t-Bu), 1.23—1.54 (2H, m, CH_2 of Et), 2.57—2.67 (1H, m, H-1′), 2.92 (1H, dq, $J_{2'-1'}$=4.8 and $J_{2'-Me}$=7.0 Hz, H-2′), 3.49 (1H, d, $J_{2-1'}$=8.1 Hz, H-2), 3.73, 3.75 (each 3H, each s, COOMe), 6.21 (1H, d, J_{trans}=16.1 Hz, H-4′), and 6.93 (1H, d, J_{trans}=16.1 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ=11.46 (Et), 12.90 (2′-Me), 21.48 (Et), 28.74 (*t*-Bu), 33.81 (*t*-Bu), 41.08 (C-1′), 45.73 (C-2′), 52.38, 52.48 (each COOMe), 54.44 (C-2), 123.71 (C-4′), 157.52 (C-5′), 169.27, 169.35 (each COOMe), and 202.87 (C-3′); MS *m/z* (rel intensity, %) 313 (M^++1, 2), 312 (M^+, 7), 181 (12), 140 (91), and 111 (base peak). Found: C, 65.36; H, 8.87%. Calcd for $C_{17}H_{28}O_5$: C, 65.34; H, 9.04%.

Dimethyl [(*E*)-2,6,6-Trimethyl-1-phenyl-3-oxo-4-heptenylidene]malonate (13d): Only *anti*-isomer was isolated and purified by column chromatography on silica gel with hexane–EtOAc (15 : 1, v/v). Pale yellow liquid; IR (neat) 2950, 1750, 1730, 1620, 1430, and 1160 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.98 (9H, s, *t*-Bu), 1.14 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 3.40 (1H, dq, $J_{2'-Me}$=7.0 and $J_{2'-1'}$=7.3 Hz, H-2′), 3.46, 3.71 (each 3H, each s, COOMe), 3.75 (1H, dd, $J_{1'-2'}$=7.3 and $J_{1'-2}$=8.8 Hz, H-1′), 4.01 (1H, d, $J_{2-1'}$=8.8 Hz, H-2), 5.83 (1H, d, J_{trans}=15.8 Hz, H-4′), 6.69 (1H, d, J_{trans}=15.8 Hz, H-5′), and 7.20 (5H, s, Ph); ^{13}C NMR ($CDCl_3$) δ=15.31 (2′-Me), 28.61 (*t*-Bu), 33.69 (*t*-Bu), 47.26 (C-2′), 47.92 (C-1′), 52.28, 52.55 (each COOMe), 54.92 (C-2), 123.97 (C-4′), 127.18, 128.09, 129.15, 139.03 (each Ph), 157.19 (C-5′), 168.37, 168.86 (each COOMe), and 202.30 (C-3′); MS *m/z* (rel intensity, %) 361 (M^++1, 9), 360 (M^+, 34), 328 (11), 269 (12), 230 (10), 229 (54), 140 (16), and 111 (base peak). HRMS Found: *m/z* 360.1939. Calcd for $C_{211}H_{28}O_5$: M, 360.1935.

Dimethyl [(*E*)-1-*t*-Butyl-2,6,6-trimethyl-3-oxo-4-heptenylidene]malonate (13e): Only *anti*-isomer was isolated and purified by column chromatography on silica gel with hexane–EtOAc (15 : 1, v/v). *anti*-isomer: Pale yellow liquid; IR (neat) 2950, 1730, 1620, 1430, 1350, and 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.88, 1.10 (each 9H, each s, *t*-Bu), 1.12 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 3.00 (1H, dd, $J_{1'-2}$=3.3 and $J_{1'-2'}$=8.8 Hz, H-1′), 3.30 (1H, dq, $J_{2'-Me}$=7.0 and $J_{2'-1'}$=8.8 Hz, H-2′), 3.74 (6H, s, 2×COOMe), 3.81 (1H, d, $J_{2-1'}$=3.3 Hz, H-2), 6.10 (1H, d, J_{trans}=16.1 Hz, H-4′), and 6.90 (1H, d, J_{trans}=16.1 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ=16.57 (2′-Me), 28.74, 29.17 (each *t*-Bu), 33.79, 35.02 (each *t*-Bu), 43.92 (C-1′), 48.49 (C-2′), 50.81 (C-2), 52.19, 52.61 (each COOMe), 123.88 (C-4′), 157.09 (C-5′), 170.17, 171.37 (each COOMe), and 203.52 (C-3′), MS *m/z* (rel intensity, %) 341 (M^++1, 2), 340 (M^+, 7), 283 (16), 242 (10), 208 (15), and 111 (base peak). Found: C, 67.22; H, 9.28%. Calcd for $C_{19}H_{32}O_5$: C, 67.01; H, 9.48%.

Dimethyl [(*E*)-1-Ethyl-2-methyl-3-oxo-4-hexenylidene]malonate (13f): Obtained as a 64 : 36 inseparable mixture of *anti*-**13f** and *syn*-**13f** (by ^{1}H NMR) after column chromatography on silica gel using hexane–EtOAc (10 : 1 to 15 : 1, v/v). Pale yellow liquid: IR (neat) 2900, 1720, 1690, 1620, 1420, 1190, and 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$) *anti*-isomer δ=0.92 (3H, t, *J*=7.3 Hz, 1′-Et), 1.06 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 1.24—1.58 (2H, m, 1′-Et), 1.91 (3H, dd, $J_{6'-4'}$=1.8 and $J_{6'-5'}$=7.0 Hz, H-6′), 2.53—2.68 (1H, m, H-1′), 2.99 (1H, dq, $J_{2'-1'}$=$J_{2'-Me}$=7.0 Hz, H-2′), 3.56 (1H, d, $J_{2-1'}$=6.2 Hz, H-2), 3.69, 3.73 (each 3H, each s, COOMe), 6.21 (1H, dq, $J_{4'-6'}$=1.8 and J_{trans}=15.8 Hz, H-4′), and 6.89 (1H, dq, $J_{5'-6'}$=7.8 and J_{trans}=15.8 Hz, H-5′); *syn*-isomer δ=0.82 (3H, t, *J*=7.3 Hz, 1′-Et), 1.02 (3H, d, $J_{Me-2'}$=7.0 Hz, 2′-Me), 1.24—1.58 (2H, m, 1′-Et), 1.92 (3H, dd, $J_{6'-4'}$=1.8 and $J_{6'-5'}$=7.0 Hz, H-6′), 2.53—2.68 (1H, m, H-1′), 2.89 (1H, dq, $J_{2'-1'}$=4.4 and $J_{2'-Me}$=7.0 Hz, H-2′), 3.49 (1H, d, $J_{2-1'}$=8.1 Hz, H-2), 3.73, 3.76 (each 3H, each s, COOMe), 6.34 (1H, dq, $J_{4'-6'}$=1.8 and J_{trans}=15.8 Hz, H-4′), and 6.96 (1H, dq, $J_{5'-6'}$=7.0 and J_{trans}=15.8 Hz, H-5′); ^{13}C NMR ($CDCl_3$) *anti*-isomer δ=12.69 (Et), 12.96 (2′-Me), 18.30 (C-6′), 23.90 (Et), 41.83 (C-1′), 45.08 (C-2′), 52.31, 52.35, 52.40 (COOMe and C-2), 130.68 (C-4′), 142.73 (C-5′), 169.32, 169.56 (each COOMe), and 202.30 (C-3′); *syn*-isomer δ=11.07 (Et), 12.80 (2′-Me), 18.30 (C-6′), 21.44 (Et), 40.95 (C-1′), 45.43 (C-2′), 52.45, 52.54 (each COOMe), 54.53 (C-2), 130.25 (C-4′), 142.95 (C-5′), 169.28, 169.40 (each COOMe), and 201.97 (C-3′); MS *m/z* (rel intensity, %) 271 (M^++1, 3), 270 (M^+, 15), 139 (27), 98 (base peak), and 69 (41). HRMS Found: *m/z* 270.1467. Calcd for $C_{14}H_{22}O_5$: M, 270.1466.

Catalytic Hydrogenation Followed by $Zn(BH_4)_2$ Reduction of 13d Leading to 15 and 16. A solution of **13d** (0.67 g, 1.86 mmol) in EtOH (10 ml) in the presence of palladium/carbon (10 wt%) was stirred under hydrogen at room temperature for 12 h. The catalyst was filtered off through cerite and the filtrate was evaporated in vacuo to give **14** (0.679 g, 100%) as colorless oil [**14:** IR (neat) 2950, 1710, 1430, 1230, 1150, and 1010 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.74 (9H, s, *t*-Bu), 1.14 (3H, d, $J_{Me-2'}$=7.3 Hz, 2′-Me), 1.12—1.26 (2H, m, H-5′), 1.97—2.21 (2H, m, H-4′), 3.15 (1H, dq, $J_{2'-Me}$=7.3 and $J_{2'-1'}$=7.7 Hz, H-2′), 3.47, 3.71 (each 3H, each s, COOMe), 3.73 (1H, dd, $J_{1'-2'}$=7.7 and $J_{1'-2}$=9.2 Hz, H-1′), 4.03 (1H, d, $J_{2-1'}$=9.2 Hz, H-2), and 7.15—7.29 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=14.92 (3-Me), 29.01 (*t*-Bu), 29.63 (*t*-Bu), 36.66 (C-5′), 37.87 (C-4′), 47.79, 49.70 (C-1′ and C-2′), 52.31, 52.61 (each COOMe), 54.56 (C-2), 127.31, 128.29, 128.95, 139.16 (each Ph), 168.36, and 168.91 (each COOMe), and 213.43 (C-3′), MS *m/z* (rel intensity, %) 363 (M^++1, 24), 362 (M^+, base peak), 231 (79), 221 (59), and 113 (68). HRMS Found: *m/z* 362.2094. Calcd for $C_{21}H_{30}O_5$: M, 362.2092]. An ethereal solution of freshly prepared $Zn(BH_4)_2$ (0.36 M in diethyl ether, 8.3 ml, 3 mmol) was added to **14** (0.13 g, 0.375 mmol) in ether (1 ml) and the mixture was stirred at 0 °C for 21.5 h. The reaction was quenched with aqueous HCl (1 equiv) and extracted with CH_2Cl_2 (15 ml×2). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue (0.12 g) was chromatographed on silica gel with hexane–EtOAc (10 : 1 to 4 : 1, v/v) to give **15** (0.046 g, 37%, 85 : 15 by ^{13}C NMR) and then **16** (0.046 g, 37%, 78 : 22 by ^{13}C NMR).

Methyl *c*-5-Methyl-*t*-6-(3,3-dimethylbutyl)-*r*-4-phenyl-2-oxoperhydropyran-3-carboxylate (15): Only the major isomer was isolated from the mixture. Colorless solid; mp 74—77 °C; IR (KBr) 2950, 1720, 1430, 1150, and 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.80 (3H, d, J_{Me-5}=7.3 Hz, 5-Me), 0.91 (9H, s, *t*-Bu), 1.12—1.29 (2H, m, two of H-1′ and H-2′), 1.49—1.80 (2H, m, the other of H-1′ and H-2′), 2.26 (1H, ddq, J_{5-6}=4.8, J_{5-4}=5.5, and J_{5-Me}=7.3 Hz, H-5), 3.67 (1H, dd, J_{4-5}=5.5 and J_{4-3}=7.0 Hz, H-4), 3.93 (1H, d, J_{3-4}=7.0 Hz, H-3), 4.17 (1H, dt, J_{6-5}=4.8, $J_{6-1'}$=4.8, and 7.3 Hz, H-6), and 7.12—7.38 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=14.34 (5-Me), 28.75 (C-2′), 29.24 (*t*-Bu), 30.06 (*t*-Bu), 34.34 (C-1′), 38.62 (C-5), 43.86 (C-4), 51.10, 52.94 (C-3 and COOMe), 84.33 (C-6), 127.53, 128.19, 128.72, 138.09 (each Ph), 167.64, and 169.21 (C-2 and COOMe); MS *m/z* (rel intensity, %) 332 (M^+, 75), 288 (50), 287 (39), 273 (base peak), 214 (35), 199 (37), 190 (25), 189 (23), 162 (23), 143 (41), 131 (63), 129 (29), 118 (53), 117 (25), 103 (24), 91 (44), 69 (29), 57 (54), and 41 (33). Found: C, 72.48; H, 8.43%. Calcd for $C_{20}H_{28}O_4$: C, 72.25; H, 8.49%.

Methyl 2-Hydroxy-*c*-5-methyl-*c*-6-(3,3-dimethylbutyl)-*r*-4-phenylperhydropyran-3-carboxylate (16): Only the major isomer was isolated from the mixture. Colorless solid; mp

132—134 °C; IR (KBr) 3300, 2850, 1680, 1420, 1250, 1060, and 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.68 (3H, d, J_{Me-5}=7.0 Hz, 5-Me), 0.89 (9H, s, *t*-Bu), 1.08—1.81 (5H, m, H-1′, H-2′, and H-5), 3.05 (1H, dd, J_{3-2}=8.1 and J_{3-4}=12.5 Hz, H-3), 3.37 (1H, dd, J_{4-5}=4.0 and J_{4-3}=12.5 Hz, H-4), 3.53 (3H, s, COOMe), 3.69—3.75 (1H, m, H-6), 4.96 (1H, d, J_{2-3}=8.1 Hz, H-2), and 7.10—7.33 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=6.41 (5-Me), 27.63 (C-2′), 29.30 (*t*-Bu), 30.14 (C-1′), 37.02 (*t*-Bu), 39.86 (C-5), 48.34 (C-3 and C-4), 51.86 (COOMe), 80.11 (C-6), 97.79 (C-2), 126.69, 128.06, 128.29, 140.14 (each Ph), and 172.98 (COOMe); MS *m/z* (rel intensity, %) 334 (M^+, 2), 288 (29), 209 (15), 164 (16), 163 (base peak), 162 (34), and 118 (13). Found: C, 71.77; H, 8.88%. Calcd for $C_{20}H_{30}O_4$: C, 71.81; H, 9.05%.

Demethoxycarbonylation of 15 (or 16) Leading to 17 (or 18). To a solution of **15** (0.046 g, 0.138 mmol) in MeOH (1.5 ml) was added dropwise at room temperature aqueous NaOH (3%, 1 ml). This solution was stirred for 2 h, poured into aqueous HCl (1N), and extracted with dichloromethane (10 ml×3). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was chromatographed on silica gel with hexane–EtOAc (3 : 1, v/v) to give **17** (0.025 g, 66%). A similar procedure using **16** (0.046 g, 0.137 mmol) gave **18** (0.041 g, 93%).

***c*-5-Methyl-*t*-6-(3,3-dimethylbutyl)-*r*-4-phenyl-2-oxoperhydropyran (17):** Pale yellow liquid; IR (neat) 2900, 1710, 1450, 1360, 1210, 990, 750, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.82 (3H, d, J_{Me-5}=7.0 Hz, 5-Me), 0.89 (9H, s, *t*-Bu), 1.12—1.80 (4H, m, H-1′ and H-2′), 2.14 (1H, ddq, J_{5-4}=4.8, J_{5-6}=7.0, and J_{5-Me}=7.0 Hz, H-5), 2.79—2.92 (2H, m, H-3), 3.29 (1H, m, H-4), 4.07 (1H, ddd, $J_{6-1'}$=4.0, 7.8, and J_{6-5}=7.0 Hz, H-6), and 7.11—7.38 (5H, m, Ph); NOE: H-4/H-5, 4-Ph/5-Me, and 4-Ph/H-6; ^{13}C NMR ($CDCl_3$) δ=14.53 (5-Me), 28.74 (C-2′), 29.26 (*t*-Bu), 30.05 (*t*-Bu), 34.50 (C-1′) 35.61 (C-5), 38.56 (C-4), 40.53 (C-3), 83.24 (C-6), 127.15, 128.15, 128.52, 139.59 (each Ph), and 171.57 (C-2); MS *m/z* (rel intensity, %) 275 (M^++1, 7), 274 (M^+, 32), 142 (22), 131 (27), 118 (base peak), 104 (28), and 91 (22). HRMS Found: *m/z* 274.1933. Calcd for $C_{18}H_{26}O_2$: M, 274.1931

***c*-5-Methyl-*c*-6-(3,3-dimethylbutyl)-*r*-4-phenyl-2-oxoperhydropyran (18):** Pale yellow solid; mp 85—87 °C; IR (KBr) 2950, 1720, 1450, 1360, 1220, 1060, 990, and 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.72 (3H, d, J_{Me-5}=7.0 Hz, 5-Me), 0.91 (9H, s, *t*-Bu), 1.12—1.84 (4H, m, H-1′ and H-2′), 2.19 (1H, ddq, J_{5-4}=3.5, J_{5-Me}=7.0, and J_{5-6}=10.1 Hz, H-5), 2.79 (1H, ddd, J_{3eq-5}=0.7, J_{3eq-4}=6.6, and J_{gem}=18.3 Hz, H-3_{eq}), 2.92 (1H, dd, J_{3ax-4}=12.5, J_{gem}=18.3 Hz, H-3_{ax}), 3.41 (1H, ddd, J_{4-5}=3.5, J_{4-3eq}=6.6, and J_{4-3ax}=12.5 Hz, H-4), 4.44—4.50 (1H, m, H-6), and 7.18—7.40 (5H, m, Ph); NOE: H-3_{ax}/Ph, H-3_{eq}/H-4, H-4/H-5, H-4/H-6, and H-5/H-6; ^{13}C NMR ($CDCl_3$) δ=4.95 (5-Me), 28.06 (C-2′), 29.24 (*t*-Bu), 29.69 (*t*-Bu), 30.08 (C-1′), 35.98 (C-5), 39.48 (C-4), 41.83 (C-3), 85.50 (C-6), 127.07, 128.66, 140.30 (each Ph), and 170.98 (C-2); MS *m/z* (rel intensity, %) 275 (M^++1, 3), 274 (M^+, 15), 119 (11), 118 (base peak), and 104 (10). Found: C, 78.58; H, 9.35%. Calcd for $C_{18}H_{26}O_2$: C, 78.78; H, 9.56%.

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