

Regioselective Robinson Annulation Realized by the Combined Use of Lithium Enolates and Aluminum Tris(2,6-diphenylphenoxide) (ATPH)

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Michael addition of lithium enolates derived from ketones to a variety of α,β -unsaturated ketones was realized in the presence of aluminum tris(2,6-diphenylphenoxide) (ATPH). In this reaction, ATPH can be used as a carbonyl protector of α,β -unsaturated carbonyl substrates upon complexation, which facilitates the regioselective 1,4-addition of lithium enolates to Michael acceptors. Similarly, dianions of β -dicarbonyl compounds undergo Michael addition smoothly using ATPH as an effective promoter of the reaction. Subsequent regioselective, intramolecular aldol condensation was also demonstrated, leading to bicyclic carbon ring systems. Such systems are difficult to obtain by the Robinson annulation usually performed in protic media.

The Robinson annulation,¹⁾ with its subsequent modification,²⁾ is one of the most powerful tools for the synthesis of natural products which include steroidal skeletons.³⁾ This annulation system consists of two distinct reaction steps: (1) intermolecular Michael addition of a ketone enolate and (2) intramolecular aldol condensation (Chart 1). The regioselectivity of the initial Michael addition ("thermodynamic" enolate (A) over "kinetic" enolate (B)) and that of the subsequent annulation (dehydration at the carbonyl of a Michael donor moiety (C) over that of a Michael acceptor moiety (D)) are controlled by thermodynamic factors. Accordingly, the reactions for obtaining regioselectivities opposite to those with Robinson annulation are minor processes⁴⁾ under protic conditions. The Lewis acid-promoted Michael addition of silyl enol ethers to α -enones⁵⁾ or their acetal derivatives,⁶⁾ originally devised by Mukaiyama et al. with its variant,⁷⁾ is a useful method for promoting "kinetic" enolate additions. In contrast to the great value of silyl enol ethers as Michael donors, lithium enolates have received considerably less attention for this purpose presumably due to their high reactivity to undergo undesired side reactions:⁸⁾ i.e., proton transfer, 1,2-addition, and polymerization.

We recently showed that the Michael addition of carbanions toward several α,β -unsaturated carbonyl compounds could be achieved by the complete blocking of carbonyl functions in these substrates with aluminum tris(2,6-diphenylphenoxide) (ATPH).⁹⁾ In these reactions, ATPH acted as a receptor to bind carbonyls, inhibiting the attack of the nucleophiles in a 1,2-manner with the cooperation of ATPH ligands. Continuation of our work on ATPH-assisted 1,4-

addition to α,β -unsaturated ketones led us to an annulation, which appears to be promising for the control of "kinetic" enolate addition (B), followed by an alternative ring closure involving dehydration at the carbonyl of a Michael donor moiety (C) or of a Michael acceptor moiety (D). We reported here the Michael addition of lithium enolates which include dianions β -dicarbonyl compounds to α,β -unsaturated ketones by complexation with ATPH, which enables regioselective annulation (Scheme 1).

Michael Addition of Lithium Enolates to α -Enones. We first examined the possibility of the Michael addition of ketone enolates to 2-cyclopenten-1-one (**1**) in the presence of ATPH. Treatment of **1** with ATPH at -78°C in CH_2Cl_2 , followed by addition of the lithium enolate of benzylideneacetone (**7**) (LDA, THF, -78°C for 5 min) at this temperature, gave Michael adduct **8a** in an isolated yield of 90% (Chart 2). Reaction of the same enolate with 6-, 7-, and 8-membered enones **3**, **4**, and **5** was also successful and gave the corresponding 1,4-addition products **8b**, **8c**, and **8d** in high yields. This method can be generally extended to other ketone enolates, regardless of the attached substituents under similar reaction conditions. The results are outlined in Table 1. It is worth emphasizing that a trace amount of 1,2-addition products was produced upon reaction with cyclic Michael acceptors (< 1%). The 1,4-addition of lithium enolate of acetone to chalcone (**6**) occurred more regioselectively when we replace the solvent used to prepare the lithium enolate with 1,2-dimethoxyethane (DME) (56%; **14**: 1,2-adduct = 6.2:1).

Synthesis of Octalone Derivatives. The reaction of *trans*-3-penten-2-one (**15**) with the lithium enolate of cyclohexanone (**16**) (LDA, THF; -78°C) in the presence of ATPH in CH_2Cl_2 at -78°C gave a mixture of the stereoisomers in

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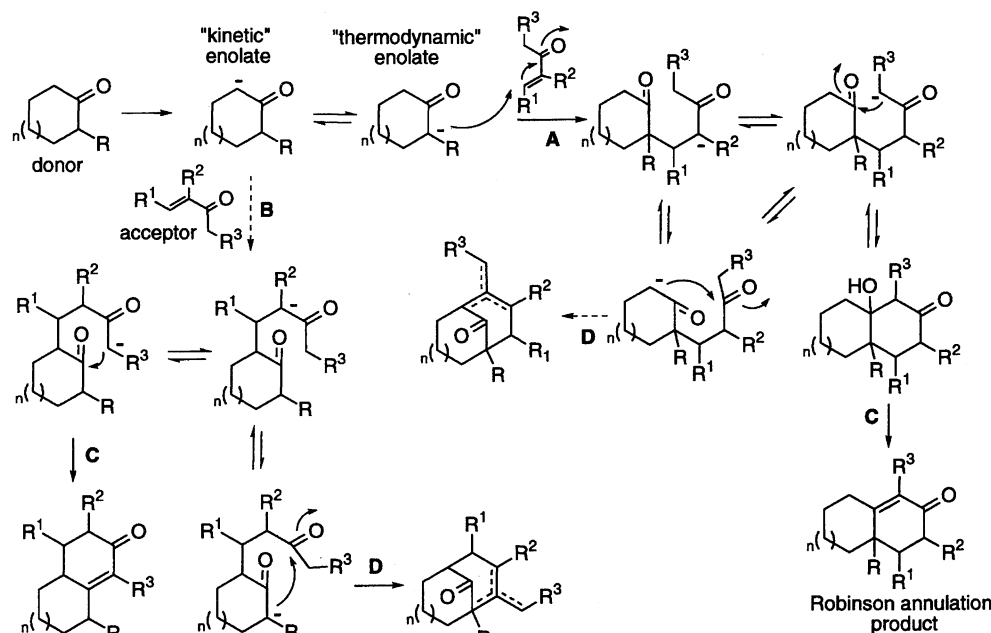
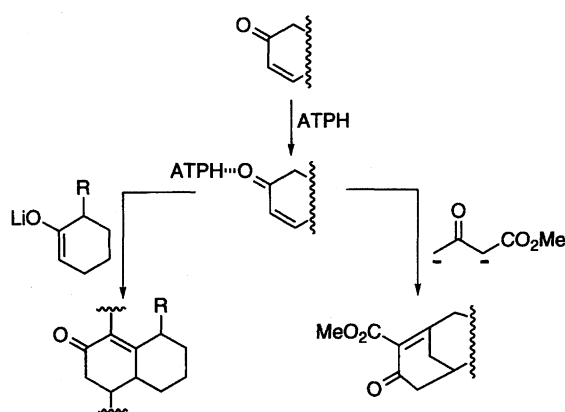


Chart 1.



Scheme 1.

80% yield (**17a**: **17b**=87:13). This stereochemical outcome is different from those of the $\text{Bu}_2\text{Sn}(\text{OTf})_2^{78)}$ - and $\text{TiCl}_4\text{-Ti}(\text{OPr}^i)_4^{10)}$ -mediated Michael additions of the corresponding silyl enol ether, which give Michael adducts **17a** and **17b** in ratios of 50:50 and ca. 83:17, respectively. The resulting isomeric products were subjected to subsequent cyclization under basic conditions (KOH, EtOH; reflux, 1 h) to give annulated octahydronaphthalenones (*cis* and *trans* isomers **18a** and **18b**) in 50% yield in a ratio of 88:12. The reaction of Stork's α -silylated enone¹¹⁾ **19** with the "kinetic" enolate of 2-methylcyclohexanone (**20**) also proceeded in the presence of ATPH to give diastereomers **21a** and **21b** in a ratio of ca. 1:1.¹²⁾ Treatment of the ATPH/3-methyl-3-buten-2-one (**22**) complex with lithium enolate **20** under similar conditions, followed by capture of the resulting enolate with methyl trifluoromethanesulfonate (MeOTf) at -78°C , gave 1,4-adduct **23** as a mixture of *trans* and *cis* isomers (66:34), which were transformed into decalones **24a** and **24b** in 78% yield in a ratio of 66:34 (Scheme 2).¹²⁾

Michael Addition of the Dianions of β -Dicarbonyl

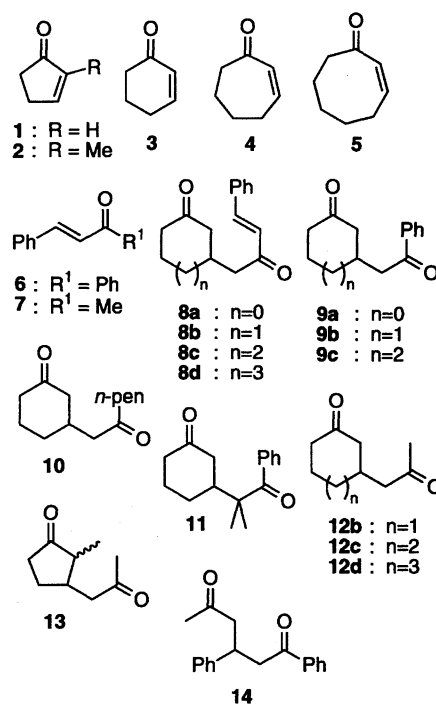
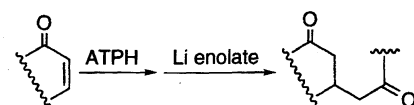


Chart 2.

Compounds. The nucleophilic addition of dianions of β -dicarbonyl substrate to α,β -unsaturated carbonyl compounds is known to proceed in a 1,2-fashion.¹³⁾ Michael addition of a β -keto ester dianion proceeded smoothly using ATPH. Treatment of α -enone **6** or **7** with ATPH in CH_2Cl_2 at -78°C was followed by addition of dianion **25** prepared by treatment of methyl acetoacetate with NaH and *n*-BuLi at 0°C in THF. After stirring for 30 min and subsequent quenching with 1 M HCl (1 M = 1 mol dm^{-3}), annulation products **26** and **27** were formed in yields of 80 and 94%, respectively. The generated enolate intermediate could be

Table 1. Michael Addition of Lithium Enolates to α,β -Unsaturated Ketones^{a)}


Entry	Ketone enolates ^{b)}	Enone	Conditions °C, h	Product	Yield % ^{c)}
1		1	-78, 1	8a	90
2		3	-78, 0.3	8b	90
3		4	-78, 0.3	8c	71 ^{e)}
4		5	-78, 0.3	8d	87 ^{e)}
5		1	-78, 0.1	9a	86
6		3	-78, 1.5	9a	98
7		4	-78, 0.1	9c	85
8		3	-78, 1	10	84 ^{e)}
9		3	-90, 0.3	11	75 ^{e)}
10		2	-78, 1	13^{g)}	85
11		3	-78, 0.3	12b	64
12		4	-78, 0.3	12c	73 ^{e)}
13		5	-78, 0.3	12d	83 ^{e)}
14		6	-78, 1	14	72 ^{f)}

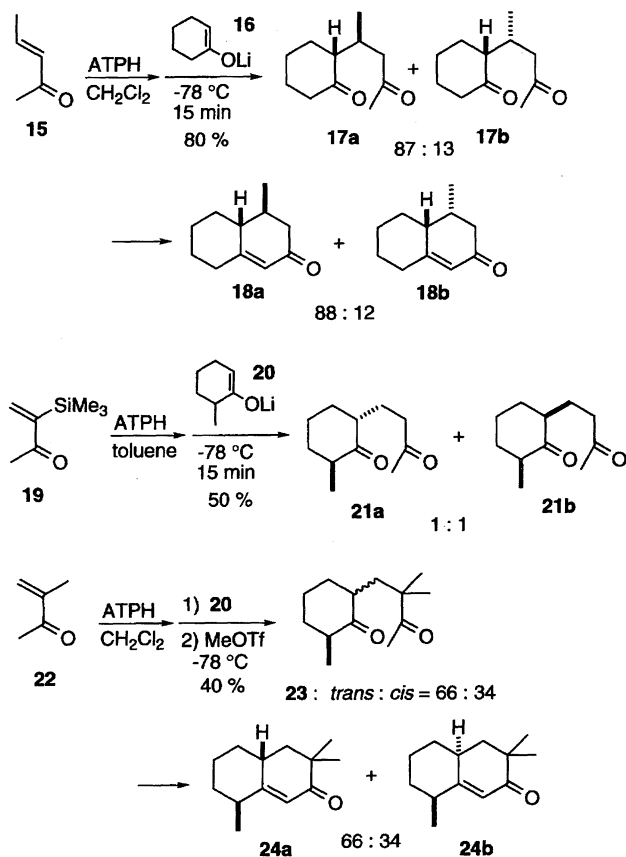
a) Unless otherwise noted, the ATPH (1.1 equiv)-enone (1 equiv) complex in CH_2Cl_2 was treated with a Li enolate (1.1–4.0 equiv) in THF. b) Li enolate was generated by treatment of the corresponding ketone with LDA. c) Of isolated, purified product. d) Generated from the corresponding silyl enol ether and MeLi in THF at 0 °C. e) Toluene was used in place of CH_2Cl_2 . f) 16% of 1,2-adduct was obtained. g) *Trans* : *cis* = 89 : 11.

readily trapped with MeOTf to give **28** (80%), but with a lack of diastereoselection (*cis* : *trans* = 1 : 1) after treatment with a catalytic amount of *p*-TsOH. A combination of the dianion of methyl 3-oxopentanoate with Michael acceptor **7** also gave cyclized product **29** in 43% yield in a *trans* : *cis* ratio of 1 : 1. No cyclization was observed in the reaction of **6** with dianion **30**, but the Michael addition proceeded smoothly to give **31** in 52% yield (Scheme 3, Eq. 1).

The dianion of β -diketone, acetylacetone, similarly underwent 1,4-addition to **7** to give a mixture of the annulated and nonannulated product, which could be readily converted into product **32** in 70% yield after treatment with a catalytic amount of *p*-TsOH in benzene at room temperature for 3 h (Scheme 4).

It is interesting to note that Michael addition of dianion **34** to the 'push-pull' alkene *trans*-4-methoxy-3-buten-2-one (**33**),¹⁴ followed by double-bond isomerization, gave doubly conjugated **35** as a sole product in 50% yield with an *E/Z* ratio of > 95 : 5; this was confirmed by NOESY experiment. The Michael reaction of dianion **34** with α -silylated enone **19** produced desilylated 1,4-adduct **36** in 56% yield (Scheme 5).

Annulation of Michael Adducts Derived from β -Keto Esters. An important characteristic of the aldol reac-

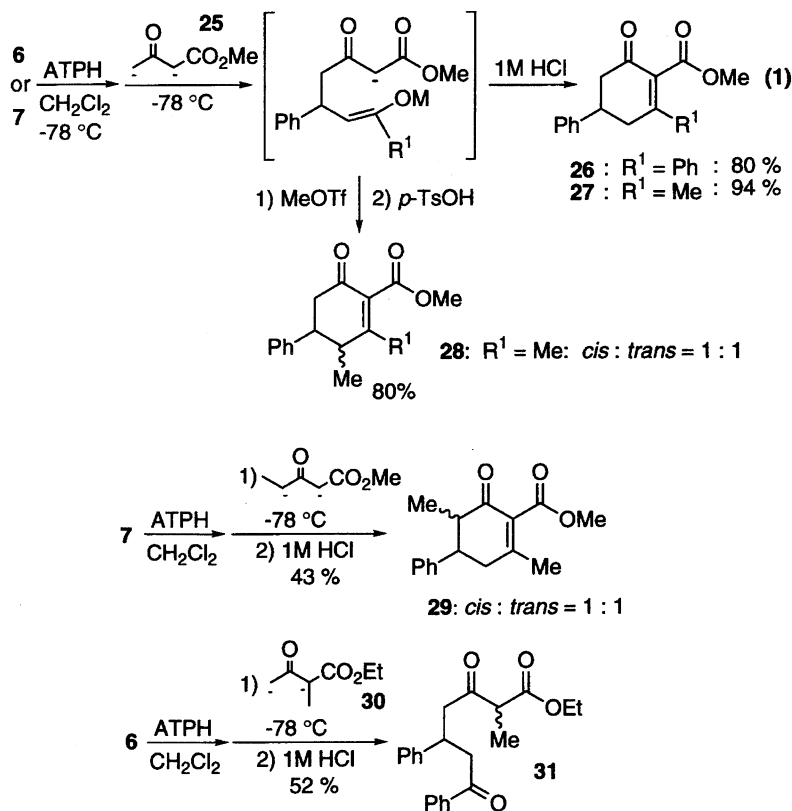


Scheme 2.

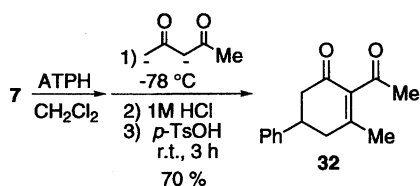
tion is the reversibility in the enolate addition step.^{15,16} The main structural factor that favors reversibility is steric compression, e.g. branching at the hydroxy carbon in the aldol. In fact, cyclization proceeded smoothly to give **26** or **27** (Scheme 3, Eq. 1), whereas the reaction of α -enone **37** with dianion **25** and MeOTf gave no annulation products after a similar acidic work up. Thus, Michael adduct **38** with the sterically congested *gem*-methyl groups was solely obtained in an isolated yield of 80% (Scheme 6).

To establish a smooth and regioselective aldol cyclization for Michael adducts derived by dianion additions, we selected **38** as a model substrate which could give two possible cyclization products (Scheme 6). Aldol cyclization using MeONa, Bu₄NOH, and RbOH in MeOH led to a mixture of two annulation products **39** and **40** in ratios of 63 : 37, 89 : 11, 77 : 23, respectively (Entries 2, 3, and 4; Table 2). The use of a catalytic amount of *p*-TsOH in benzene upon reflux gave product **40** almost exclusively (Entry 1; Table 2). This result suggests the striking influence of the two *gem*-methyl groups on dehydration at the carbonyl of the Michael donor moiety. On the other hand, the regiochemically opposite annulation was achieved by using 5 equiv of TiCl₄ to give **39** as a sole product in a quantitative yield (Entry 5; Table 2).

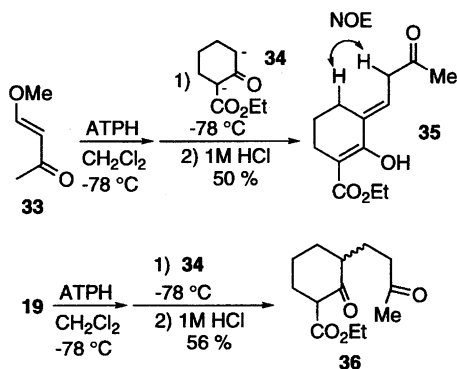
This remarkable preference of the β -keto ester moiety of **38** for undergoing intramolecular nucleophilic addition can be best explained by the intervention of the chelation complex with TiCl₄. Activation of the sterically more encumbered carbonyl with TiCl₄ also promotes sequential enolate



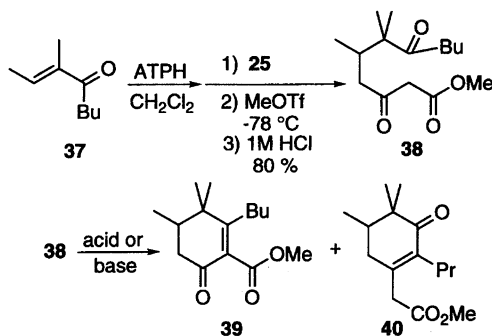
Scheme 3.



Scheme 4.



Scheme 5.



Scheme 6.

Table 2. Cyclization of Michael Adduct 38 with Various Reagents

Entry	Reagent	39 : 40	Yield
1	<i>p</i> -TsOH	<1 : >99	73%
2	MeONa/MeOH	63 : 37	64%
3	Bu ₄ NOH/MeOH	89 : 11	53%
4	RbOH/MeOH	77 : 23	62%
5	TiCl ₄	>99 : <1	100%

addition and dehydration (Scheme 7).

Based on these findings, construction of bicyclo[5.3.1]-undecane carbon frameworks, which can also be seen in the AB rings of the taxol family,¹⁷⁾ becomes possible. Complexation of 2-cycloocten-1-one (5) with ATPH at -78°C , followed by addition of the dianion of ethyl acetoacetate, gave, after 30 min, Michael adduct 42 in 70% yield. Subse-

quent treatment of adduct 42 with TiCl_4 in CH_2Cl_2 at room temperature for 3 h gave the desired bicyclo[5.3.1]undecane compound 44 in an isolated yield of 94%. This method was extended to α -methyl substrate 43 (*cis* : *trans* => 8 : 1, determined by NOESY experiment) to give 45 in 89% yield with a *cis* : *trans* ratio of > 99 : 1. The desired cyclization of Michael adduct 42 was achieved even with *p*-TsOH, while

Scheme 7.

Scheme 8.

throughout this work, Merck precoated TLC plates (silica gel 60 GF254 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel (E. Merck Art. 9385). Microanalyses were accomplished at the Faculty of Agriculture, Nagoya University.

In experimental which require dry solvents, CH_2Cl_2 and toluene were freshly distilled from calcium hydride, and tetrahydrofuran (THF) and 1,2-dimethoxyethane (DME) were freshly distilled from sodium metal using benzophenone ketyl as indicator. With the following exceptions, the organic substrates **1**, **2**, **3**, **6**, **7**, **15**, **22**, **33**, and acetophenone, 2-octanone, isobutyrophenone, acetone, methyl acetoacetate, methyl 3-oxopentanoate, ethyl 2-oxocyclohexanecarboxylate, acetylacetone, and ethyl 2-methyl-3-oxobutyrates were all commercially available, and were distilled or recrystallized before use. *n*-BuLi (hexane solution) was obtained from Mitsuwa. 3-Penten-2-one (**15**) (65% purity, Tokyo Kasei) was purified by column chromatography on silica gel before use. The Stork's α -silylated enone (**19**),^{11b} 2-cyclohepten-1-one (**4**),¹⁸ 2-cycloocten-1-one (**5**),¹⁸ 2-methyl-2-cycloocten-1-one (**41**),¹⁹ 2-(trimethylsiloxy)-1-octene,²⁰ and 2-(trimethylsiloxy)-1-propene²¹ were prepared as described in the literature procedure. Diketones **17**^{7s}, **18**^{10,22} and **21**¹² are all known compounds.

Preparation of ATPH. To a solution of 2,6-diphenylphenol (3 equiv) in toluene was added at room temperature a 1.0 M hexane solution of Me_3Al (1 equiv). The methane gas (ca. 3 equiv) evolved immediately. The resulting pale yellow solution was stirred at room temperature for 0.5 h and used without further purification.

General Procedure for Conjugate Addition of Ketone Lithium Enolates to α,β -Unsaturated Carbonyl Compounds Complexed with ATPH. The following procedure for the reaction of 2-cyclohexene-1-one (**3**) with the lithium enolate of benzylideneacetone is representative. To a solution of ATPH (0.55 mmol) in CH_2Cl_2 (5.0 mL) was added **3** (48.4 μL , 0.50 mmol) at -78°C under argon. After 5 min, the lithium enolate, generated by treatment of benzylideneacetone (292 mg, 2.0 mmol) with a THF (3.0 mL) solution of LDA (2.0 mmol) at -78°C for 15 min, was transferred by a cannula to the CH_2Cl_2 solution of ATPH-**3** complex at -78°C . The reaction mixture was stirred at this temperature for 15 min, quenched with 1.0 M HCl, and extracted with ether. The organic layer was dried over Na_2SO_4 , and concentrated. The residue was purified by column chromatography on silica gel (ether/hexane = 1/4 to 1/2 to 1/1 to 1/0 as the eluent) to give **8b** (108.8 mg, yield 90%) as a white solid. 2,6-Diphenylphenol could be recovered in more than 90% yield.

3-(2-Oxo-4-phenyl-3-butenyl)cyclopentanone (8a). IR (KBr) 2897, 1744, 1659, 1508, 1491, 1374, 1237, 1181, 1159, 970, 752, 692 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.57 (d, 1H, J = 16.5 Hz, PhCH), 7.60–7.30 (m, 5H, C_5H_5), 6.75 (d, 1H, J = 16.2 Hz, PhCHCH), 2.94–2.10 (m, 7H), 1.96–1.48 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 218.7, 198.6, 142.9, 134.3, 130.7, 129.0, 128.3, 126.0, 46.1, 44.8, 38.3, 32.7, 29.4. Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_2$: C, 78.92; H, 7.06%. Found: C, 78.88; H, 7.01%.

3-(2-Oxo-4-phenyl-3-butenyl)cyclohexanone (8b). IR (KBr) 2932, 1701, 1686, 1610, 1495, 1373, 1279, 1115, 1061, 990, 745, 689 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.55 (d, 1H, J = 16.2 Hz, PhCH), 7.62–7.30 (m, 5H, C_5H_5), 6.73 (d, 1H, J = 16.2 Hz, PhCHCH), 2.83–1.84 (m, 9H), 1.84–1.33 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 210.6, 198.3, 142.9, 134.3, 130.6, 129.0, 128.3, 126.2, 47.7, 46.9, 41.2, 34.9, 31.0, 24.9. Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_2$: C, 79.31; H, 7.49%. Found: C, 79.29; H, 7.55%.

3-(2-Oxo-4-phenyl-3-butenyl)cycloheptanone (8c). IR (KBr) 2855, 1692, 1613, 1451, 1399, 1138, 1068, 752, 693 cm^{-1} ;

^1H NMR (CDCl_3 , 300 MHz) δ = 7.56 (d, 1H, J = 16.2 Hz, PhCH), 7.60–7.30 (m, 5H, C_5H_5), 6.75 (d, 1H, J = 16.2 Hz, PhCHCH), 2.80–2.38 (m, 7H), 2.00–1.80 (m, 3H), 1.75–1.24 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 213.4, 198.5, 142.7, 134.2, 130.5, 128.9, 128.2, 126.2, 49.6, 47.6, 43.8, 36.5, 31.8, 28.4, 24.3. Anal. Calcd for $\text{C}_{17}\text{H}_{20}\text{O}_2$: C, 79.65; H, 7.86%. Found: C, 79.60; H, 7.91%.

3-(2-Oxo-4-phenyl-3-butenyl)cyclooctanone (8d). IR (neat) 2930, 1698, 1659, 1611, 1576, 1495, 1449, 1331, 1195, 1075, 980, 918, 750, 691 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.56 (d, 1H, J = 16.2 Hz, PhCH), 7.63–7.30 (m, 5H, C_5H_5), 6.76 (d, 1H, J = 16.2 Hz, PhCHCH), 2.85–2.23 (m, 7H), 2.00–1.60 (m, 4H), 1.60–1.22 (m, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 216.2, 199.0, 142.8, 134.3, 130.5, 128.8, 128.3, 126.3, 47.4, 47.1, 42.4, 33.6, 32.8, 27.2, 25.6, 23.7. Anal. Calcd for $\text{C}_{18}\text{H}_{22}\text{O}_2$: C, 79.96; H, 8.20%. Found: C, 79.96; H, 8.09%.

3-(2-Oxo-2-phenylethyl)cyclopentanone (9a). IR (KBr) 1740, 1686, 1595, 1450, 1408, 1375, 1238, 1218, 1202, 1161, 997, 760, 692 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.96 (d, 2H, J = 7.2 Hz, *o*-CH), 7.59 (t, 1H, J = 7.2 Hz, *p*-CH), 7.48 (t, 2H, J = 7.2 Hz, *m*-CH), 3.18 (dd, 1H, J = 16.7, 6.8 Hz, CHHCOPh), 3.11 (dd, 1H, J = 16.4, 6.8 Hz, CHHCOPh), 2.82 (m, 1H), 2.58 (dd, 1H, J = 18.5, 7.6 Hz), 2.41–2.22 (m, 3H), 1.90 (dd, 1H, J = 9.3, 18.1 Hz), 1.62 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 218.6, 198.5, 136.7, 133.2, 128.6, 127.9, 44.8, 43.9, 38.3, 32.6, 29.4. Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: C, 77.20; H, 6.98%. Found: C, 77.28; H, 6.96%.

3-(2-Oxo-2-phenylethyl)cyclohexanone (9b). IR (KBr) 2953, 2918, 1714, 1682, 1595, 1445, 1404, 1277, 1265, 1229, 1190, 999, 752, 693 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.95 (d, 2H, J = 7.2 Hz, *o*-CH), 7.59 (t, 1H, J = 7.2 Hz, *p*-CH), 7.48 (t, 2H, J = 7.2 Hz, *m*-CH), 3.03 (dd, 1H, J = 16.5, 6.9 Hz, CHHCOPh), 2.94 (dd, 1H, J = 16.4, 5.9 Hz, CHHCOPh), 2.62–2.19 (m, 7H), 1.74 (m, 1H), 1.47 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 210.6, 198.3, 136.8, 133.2, 128.6, 128.0, 47.7, 44.6, 41.2, 34.8, 31.1, 24.9. Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_2$: C, 77.75; H, 7.46%. Found: C, 77.75; H, 7.30%.

3-(2-Oxo-2-phenylethyl)cycloheptanone (9c). IR (neat) 2928, 2857, 1698, 1686, 1597, 1449, 1267, 1209, 1182, 978, 752, 691 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.96 (d, 2H, J = 7.2 Hz, *o*-CH), 7.59 (t, 1H, J = 7.2 Hz, *p*-CH), 7.48 (t, 2H, J = 7.2 Hz, *m*-CH), 2.95 (d, 2H, J = 6.3 Hz, CH_2COPh), 2.65–2.40 (m, 5H), 2.00–1.82 (m, 3H), 1.72–1.28 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 213.5, 198.6, 136.9, 133.1, 128.6, 127.9, 49.7, 45.2, 43.8, 36.6, 31.7, 28.5, 24.4. Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_2$: C, 78.23; H, 7.88%. Found: C, 78.17; H, 7.86%.

3-(2-Oxoheptyl)cyclohexanone (10). IR (neat) 2929, 1713, 1449, 1377, 1344, 1227, 1129, 1057, 953, 868 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 2.53–2.17 (m, 8H), 2.13–1.83 (m, 3H), 1.82–1.63 (m, 1H), 1.56 (m, 2H), 1.45–1.17 (m, 5H), 0.89 (t, 3H, J = 6.9 Hz, CH_3); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 210.7, 209.3, 48.6, 47.4, 43.3, 41.1, 34.2, 31.2, 30.8, 24.8, 23.3, 22.3, 13.8. Anal. Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2$: C, 74.24; H, 10.54%. Found: C, 74.08; H, 10.91%.

3-(1,1-Dimethyl-2-oxo-2-phenylethyl)cyclohexanone (11). IR (neat) 2944, 2869, 1717, 1671, 1636, 1447, 1391, 1370, 1318, 1233, 1161, 965, 723, 704 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.62 (d, 2H, J = 6.8 Hz, *o*-CH), 7.55–7.35 (m, 3H, *p*-CH and *m*-CH), 2.55–1.97 (m, 6H), 1.90–1.44 (m, 3H), 1.29 (s, 6H, $(\text{CH}_3)_2$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 211.1, 208.2, 138.7, 130.9, 128.1, 127.4, 50.5, 45.0, 43.1, 41.2, 26.5, 25.1, 22.9, 21.8. Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{O}_2$: C, 78.65; H, 8.25%. Found: C, 78.20; H, 8.67%.

3-(2-Oxopropyl)cyclohexanone (12b). IR (neat) 2940, 1710, 1449, 1424, 1362, 1316, 1227, 1159, 1101, 953, 870 cm^{-1} ;

^1H NMR (CDCl_3 , 300 MHz) δ = 2.60—1.18 (m, 6H), 2.13 (s, 3H, CH_3), 2.12—1.83 (m, 3H), 1.83—1.62 (m, 1H), 1.48—1.30 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 210.6, 206.9, 49.64, 47.4, 41.1, 34.2, 30.8, 30.4, 24.8. Anal. Calcd for $\text{C}_9\text{H}_{14}\text{O}_2$: C, 70.10; H, 9.15%. Found: C, 70.01; H, 9.60%.

3-(2-Oxopropyl)cycloheptanone (12c). IR (neat) 2928, 2859, 1715, 1700, 1447, 1412, 1362, 1256, 1165 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 2.61—2.26 (m, 6H), 2.14 (s, 3H), 1.97—1.73 (m, 3H), 1.67—1.25 (m, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 213.4, 207.1, 50.1, 49.2, 43.7, 36.3, 31.1, 30.4, 28.2, 24.1. Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_2$: C, 71.39; H, 9.59%. Found: C, 71.27; H, 10.00%.

3-(2-Oxopropyl)cycloheptanone (12d). IR (neat) 2932, 2859, 1715, 1710, 1466, 1446, 1412, 1159, 1095 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 2.73—2.20 (m, 6H), 2.16 (s, 3H), 1.95—1.80 (m, 2H), 1.72—1.16 (m, 7H); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 216.1, 207.5, 50.5, 46.7, 42.4, 33.4, 32.2, 30.4, 27.1, 26.4, 23.5. Anal. Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_2$: C, 72.49; H, 9.95%. Found: C, 72.52; H, 10.32%.

trans- and cis-2-Methyl-3-(2-oxopropyl)cyclopentanone (13). *trans*- and *cis*-Compounds **13** were obtained in a ratio of 89:11 which was established by ^1H NMR analysis. The ratio and the stereostructures of these isomeric products were confirmed by the following experiment. Treatment of a mixture of the 89:11 (*trans/cis*) of diketone **13** with K_2CO_3 (excess) in MeOH at room temperature for 15 h gave *trans*- and *cis*-**13** in a ratio of 95:5. *trans*-**13**: IR (neat) 2969, 1740, 1717, 1458, 1375, 1358, 1240, $1163, 1032, 949\text{ cm}^{-1}$; ^1H NMR (CDCl_3 , 300 MHz) δ = 2.76 (dd, 1H, J = 18.0, 3.5 Hz), 2.53—2.03 (m, 5H), 2.20 (s, 3H, COCH_3), 1.83—1.67 (m, 1H), 1.48—1.27 (m, 1H), 1.06 (d, 3H, J = 6.9 Hz, CH_3); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 219.4, 207.3, 49.3, 47.7, 39.7, 36.9, 30.2, 27.2, 12.1. Anal. Calcd for $\text{C}_9\text{H}_{14}\text{O}_2$: C, 70.10; H, 9.15%. Found: C, 70.08; H, 9.28%. *cis*-**13**: ^1H NMR (CDCl_3 , 300 MHz) δ = 2.18 (s, 3H, COCH_3), 0.94 (d, 3H, $\text{C}(2)\text{HCH}_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 45.8, 43.4, 35.7, 34.9, 30.0, 25.6, 9.8. Other shift values for *cis*-**13** could not be identified.

1,3-Diphenyl-1,5-hexanedione (14). IR (KBr) 3092, 1709, 1684, 1449, 1366, 1233, 1163, 1005, 951, $744, 702\text{ cm}^{-1}$; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.93—7.16 (m, 10H, C_6H_5), 3.89 (quintet, 1H, J = 7.1 Hz, $\text{PhC}(3)\text{H}$), 3.36 (dd, 1H, J = 7.1, 16.6 Hz), 3.28 (dd, 1H, J = 7.0, 16.6 Hz), 2.94 (dd, 1H, J = 6.7, 16.5 Hz), 2.83 (dd, 1H, J = 7.4, 16.5 Hz), 2.09 (s, 3H, COCH_3); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 207.2, 198.4, 143.5, 136.7, 133.0, 128.5, 128.4, 128.0, 127.3, 126.6, 49.5, 44.7, 36.7, 30.2. Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{O}_2$: C, 81.17; H, 6.81%. Found: C, 81.00; H, 6.92%.

Annulation of Michael Adducts 17a and 17b to Decalones 18a and 18b. A 5 wt% KOH/EtOH solution (120 μL) of the 87:13 of 1,5-diketone **17a** and **17b** (29 mg, 0.16 mmol) was refluxed for 1 h. The solution was cooled, acidified with 1.0 M HCl, and extracted with ether. The organic layer was dried over Na_2SO_4 , and concentrated. The residue was purified by column chromatography on silica gel (AcOEt /hexane = 1/5 as the eluent) to give **18a** and **18b** (13 mg, yield 50%) as a colorless oil. The stereoisomeric ratios **17a/17b** and **18a/18b** were determined by ^1H NMR analysis by comparing with the ^1H NMR values of the same products in the literature.¹⁰ Annulation of a *trans* and *cis* mixture of Michael adducts **23** was similarly achieved except that **23** (70 mg, 0.33 mmol) was used to give a 78% of **24a** and **24b** as a colorless oil after column chromatography on silica gel (AcOEt /hexane = 1/8 as the eluent).

trans- and cis-2-(2,2-Dimethyl-3-oxobutyl)-6-methylcyclohexanone (23). *trans*-**23**: IR (neat) 2969, 2932, 1705, 1451, $1356, 1129, 990\text{ cm}^{-1}$; ^1H NMR (CDCl_3 , 300 MHz) δ = 2.46 (dd,

1H, J = 6.2, 14.4 Hz, $\text{C}(2)\text{CHH}$), 2.44—2.35 (m, 1H), 2.27—2.18 (m, 1H), 2.13 (s, 3H, COCH_3), 2.10—1.99 (m, 2H), 1.80—1.75 (m, 2H), 1.42—1.26 (m, 2H), 1.19 (dd, 1H, J = 3.8, 14.4 Hz, $\text{C}(2)\text{CHH}$), 1.08 (s, 6H, $\text{C}(2)(\text{CH}_3)_2$), 0.99 (d, 3H, J = 6.4 Hz, $\text{C}(6)\text{CH}_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 214.2, 213.2, 47.4, 45.5, 37.8, 37.5 (two overlapped signals), 26.7, 25.6, 25.2, 24.9, 24.3, 14.6. Anal. Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2$: C, 74.23; H, 10.55%. Found: C, 74.23; H, 10.60%. *cis*-**23**: IR (neat) 2969, 2932, 1705, 1453, 1356, 1125, 959 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 2.72—2.61 (m, 1H), 2.50—2.42 (m, 1H), 2.30 (dd, 1H, J = 8.3, 14.2 Hz, $\text{C}(2)\text{CHH}$), 2.12 (s, 3H, COCH_3), 2.00—1.84 (m, 2H), 1.77—1.71 (m, 2H), 1.68—1.58 (m, 1H), 1.54—1.45 (m, 1H), 1.41 (dd, 1H, J = 4.0, 14.1, $\text{C}(2)\text{CHH}$), 1.15 (s, 3H, $\text{C}(2)\text{CH}_3$), 1.05 (s, 3H, $\text{C}(2)\text{CH}_3$), 1.06 (d, 3H, J = 6.8 Hz, $\text{C}(6)\text{CH}_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 216.7, 213.9, 47.4, 45.4, 42.9, 40.1, 35.3 (two overlapped signals), 25.6, 25.2, 24.6, 20.7, 15.4. Anal. Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2$: C, 74.23; H, 10.55%. Found: C, 74.33; H, 10.56%.

3,3,8-Trimethyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one (24). **24a**: IR (neat) 2968, 2929, 1670, 1622, 1456, 1383, 1306, $1221, 1169, 903\text{ cm}^{-1}$; ^1H NMR (CDCl_3 , 300 MHz) δ = 5.76 (bt, 1H, J = 1.8 Hz, $\text{C}(1)\text{H}$), 2.41—2.30 (m, 1H), 2.21—2.12 (m, 1H), 1.98—1.75 (m, 4H), 1.70—1.46 (m, 3H), 1.26—1.05 (m, 1H), 1.11 (d, 3H, J = 6.6 Hz, $\text{C}(8)\text{CH}_3$), 1.09 (s, 3H, $\text{C}(3)(\text{CH}_3)$), 1.07 (s, 3H, $\text{C}(3)\text{CH}_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 205.5, 168.1, 120.0, 43.6, 40.8, 37.4, 35.8, 35.7, 35.5, 25.4, 24.7, 24.6, 17.9. Anal. Calcd for $\text{C}_{13}\text{H}_{20}\text{O}_2$: C, 81.20; H, 10.48%. Found: C, 81.19; H, 10.62%.

24b: ^1H NMR (CDCl_3 , 300 MHz) δ = 5.73 (bd, 1H, J = 2.8 Hz, $\text{C}(1)\text{H}$), 2.68—2.52 (m, 2H), 1.98—1.75 (m, 4H), 1.70—1.46 (m, 3H), 1.26—1.05 (m, 1H), 1.18 (d, 3H, J = 7.3 Hz, $\text{C}(8)\text{CH}_3$), 1.08 (s, 3H, $\text{C}(3)\text{CH}_3$), 1.06 (s, 3H, $\text{C}(3)\text{CH}_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 205.5, 168.7, 122.3, 43.7, 41.1, 37.3, 34.7, 32.3, 31.5, 24.7, 24.4, 20.7, 19.9. Anal. Calcd for $\text{C}_{13}\text{H}_{20}\text{O}_2$: C, 81.20; H, 10.48%. Found: C, 81.19; H, 10.62%.

General Procedure for Michael Addition of the Dianion of β -Dicarbonyl Compounds to α -Enones. To a CH_2Cl_2 (7.0 mL) solution of 2.0 equiv of ATPH (1.0 mmol) was added chalcone (**6**) (104 mg, 0.50 mmol) at -78°C under argon, and the resulting orange solution was stirred at this temperature for 5 min. To the mixture was transferred via a steel cannula a THF-hexane solution of the dianion of methyl acetoacetate (prepared by the treatment of a suspension of NaH (60% in oil; 66 mg, 1.65 mmol) in THF with methyl acetoacetate (162 μL , 1.5 mmol) at 0°C for 10 min, followed by addition of a 1.60 M hexane solution of *n*-BuLi (0.99 mL, 1.59 mmol) and stirring for 20 min at the same temperature^{13,23}). The reaction mixture was stirred at -78°C for 30 min, quenched with 1 M HCl and extracted with CH_2Cl_2 . The organic layer was dried over Na_2SO_4 , and concentrated. The residue was purified by column chromatography on silica gel (ether/hexane = 1/10 to 1/5 to 1/2 as the eluent) to give **26** (123 mg, yield 80%) as a colorless solid.

Methyl 6-Oxo-2,4-diphenyl-1-carboxylate (26). IR (KBr) 3043, 2958, 1736, 1663, 1620, 1447, 1433, 1375, 1319, 1233, 1061, 1017, 785, 772, 702 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.38—7.26 (m, 10H), 3.63 (s, 3H, OCH_3), 3.58—3.48 (m, 1H, PhCH), 3.00 (d, 2H, J = 8.0 Hz, $\text{C}(5)\text{H}_2$), 2.87 (dd, 1H, J = 4.7, 11.8 Hz, $\text{C}(3)\text{HH}$), 2.78 (dd, 1H, J = 12.9, 16.4 Hz, $\text{C}(3)\text{CHH}$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 194.8, 167.1, 158.7, 142.3, 138.4, 132.7, 129.7, 128.8, 128.6, 127.2, 126.6, 126.5, 52.1, 43.6, 40.0, 39.1. Anal. Calcd for $\text{C}_{20}\text{H}_{18}\text{O}_3$: C, 78.67; H, 5.61%. Found: C, 78.24; H, 6.00%.

Methyl 2-Methyl-6-oxo-4-phenyl-1-cyclohexene-1-carboxylate (27). Following the general procedure for **26** except that

substrate **7** (73 mg, 0.5 mmol) was used, compound **27** (115 mg, yield 94%) was obtained. IR (KBr) 2953, 1742, 1665, 1634, 1437, 1387, 1236, 1070, 1022, 770, 702 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.38–7.21 (m, 5H), 3.85 (s, 3H, OCH_3), 3.40–3.29 (m, 1H, C(4)H), 2.77–2.56 (m, 4H, C(3) H_2 , C(5) H_2), 2.04 (s, 3H, C(2) CH_3); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 194.4, 167.0, 159.6, 142.3, 132.6, 128.7, 127.0, 126.5, 52.1, 43.5, 39.6, 39.5, 22.1. Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_3$: C, 74.06; H, 6.21%. Found: C, 73.81; H, 6.55%.

Methyl 2,3-Dimethyl-6-oxo-4-phenyl-1-cyclohexene-1-carboxylate (trans- and cis-28). The reaction was carried out following the general procedure for **26** using substrate **7** (88 mg, 0.60 mmol), and dianion **25** generated from methyl acetoacetate (194 μL , 1.8 mmol). After treatment with dianion **25**, MeOTf (10 equiv) was added, and the reaction mixture was stirred at -78°C for 1 h. The reaction was quenched with 1.0 M HCl, extracted with ether, dried and concentrated. The residue was treated with a catalytic amount of *p*-TsOH upon reflux for 3 h in benzene to give **28** (132 mg, yield 80%). IR (neat) 3030, 2977, 1736, 1673, 1630, 1497, 1455, 1379, 1347, 1237, 1096, 1021, 912, 733, 702 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) *trans*-**28**: δ = 7.39–7.16 (m, 5H, C_6H_5), 3.85 (s, 3H, CH_3), 3.03 (dd, 1H, J = 8.3, 15.7 Hz, C(5)-HH), 2.79–2.66 (m, 3H), 2.00 (s, 3H, C=CCH $_3$), 1.14 (d, 3H, J = 7.0 Hz, C(3)CH $_3$). *cis*-**28**: δ = 7.39–7.16 (m, 5H, C_6H_5), 3.86 (s, 3H, OCH_3), 3.59 (dt, 1H, J = 4.1, 14.6 Hz, PhCH), 2.92 (dd, 1H, J = 14.7, 16.9 Hz, C(5)HH $_{\text{axial}}$), 2.62 (dd, 1H, J = 4.1, 17.0 Hz, C(5)HH $_{\text{equatorial}}$), 2.60 (dt, 1H, J = 4.1, 7.2 Hz, CHMe), 2.08 (s, 3H, C=CCH $_3$), 0.91 (d, 3H, J = 7.2 Hz, C(3)CH $_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 194.7 and 193.9, 167.3, 165.1 and 162.0, 140.6 and 142.4, 131.9 and 133.0, 128.5 and 128.7, 127.0 and 127.1, 126.5 and 126.9, 52.1, 35.6 and 46.9, 42.2 and 43.1, 41.6 and 41.2, 20.8 and 20.2, 11.6 and 16.7. Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_3$: C, 74.39; H, 7.02%. Found: C, 74.44; H, 7.36%.

Methyl 2,5-Dimethyl-6-oxo-4-phenyl-1-cyclohexene-1-carboxylate (trans- and cis-29). *trans*-**29**: IR (KBr) 2965, 1740, 1667, 1636, 1453, 1281, 1235, 1107, 1086, 982, 700 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.38–7.20 (m, 5H, C_6H_5), 3.86 (s, 3H, OCH_3), 2.97 (ddd, 1H, J = 4.6, 11.3, 12.8 Hz, C(4)H), 2.71 (dd, 1H, J = 11.3, 18.5 Hz, C(3)HH), 2.65 (bq, 1H, J = 13.2, 6.6 Hz, MeC(5)H), 2.54 (dd, 1H, J = 4.7, 18.5 Hz, C(3)HH), 2.00 (s, 3H, C(2)CH $_3$), 0.94 (d, 3H, J = 6.6 Hz, C(5)CH $_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 196.7, 167.4, 158.1, 142.1, 132.4, 128.9, 127.4, 127.2, 52.3, 47.4, 45.8, 40.5, 21.9, 12.5. Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_3$: C, 74.39; H, 7.02%. Found: C, 74.17; H, 7.18%. *cis*-**29**: IR (neat) 2975, 1732, 1671, 1636, 1453, 1383, 1238, 1107, 1090, 914, 781 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.37–7.17 (m, 5H, C_6H_5), 3.86 (s, 3H, OCH_3), 3.53 (ddd, 1H, J = 4.7, 4.7, 9.6 Hz, C(4)H), 2.88 (dd, 1H, J = 9.3, 18.0 Hz, C(3)HH), 2.76 (bq, 1H, J = 4.7, 7.2 Hz, MeC(5)H), 2.60 (dd, 1H, J = 4.7, 18.2 Hz, C(3)HH), 2.06 (s, 3H, C(2)CH $_3$), 0.94 (d, 3H, J = 7.1 Hz, C(5)CH $_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 198.4, 167.3, 158.9, 140.4, 131.6, 128.6, 127.5, 127.0, 52.3, 45.6, 42.7, 33.3, 22.3, 10.7. Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_3$: C, 74.39; H, 7.02%. Found: C, 74.40; H, 7.13%.

Ethyl 2-Methyl-3,7-dioxo-5,7-diphenylheptanoate (31). The reaction was carried out following the general procedure for **26**, except that substrate **6** (125 mg, 0.60 mmol) and dianion **30** generated from ethyl 2-methyl-3-oxobutyrates (225 μL , 1.8 mmol) were used to give **31** (165 mg, yield 78%). IR (neat) 2984, 1744, 1686, 1597, 1451, 1373, 1204, 1121, 1003, 912, 750, 700 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.93–7.17 (m, 10H, $2\times\text{C}_6\text{H}_5$), 4.15 (dq, 1H, J = 7.1, 8.3 Hz, OCHHMe), 4.10 (dq, 1H, J = 7.1, 8.3 Hz, OCHHMe), 3.93 (ddt, 1H, J = 14.1, 7.0, 3.4 Hz, PhCH), 3.54–3.24

(m, 3H), 3.04 (d, 1H, J = 6.9 Hz), 3.02 (ddd, 1H, J = 17.2, 44.2, 7.2 Hz), 1.25 (d, 3H, J = 7.1 Hz, C(2)CH $_3$), 1.22 (t, 3H, J = 7.1 Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 204.2 and 204.0, 198.3 and 198.2, 170.2 and 170.1, 143.4, 136.7, 133.0, 128.5, 128.0, 127.3, 126.6, 61.3, 53.0, and 52.9, 47.5 and 47.2, 44.5 and 44.4, 36.5 and 36.3, 14.0 and 13.9, 12.4. One overlapped signal is included. Anal. Calcd for $\text{C}_{22}\text{H}_{24}\text{O}_4$: C, 74.98; H, 6.86%. Found: C, 74.99; H, 6.89%.

2-Acetyl-3-methyl-5-phenyl-2-cyclohexen-1-one (32). The reaction was carried out following the general procedure for **26** using acetylacetone (0.19 mL, 1.5 mmol) and benzylidenacetone (73 mg, 0.50 mmol) except for the residual treatment after extraction. After the organic layer was concentrated, the residue was dissolved in benzene (4.0 mL) and was treated with a catalytic amount of *p*-TsOH upon reflux for 1 h. The mixture was quenched with aqueous NaHCO_3 , and extracted with ether. The organic layer was dried, concentrated, and the residue was purified by column chromatography on silica gel (ether/hexane = 1/5 to 1/3 to 1/1 as the eluent) to give **32** (57 mg, yield 50%) as a colorless solid. IR (KBr) 2979, 1701, 1624, 1603, 1497, 1455, 1379, 1352, 1310, 1215, 1138, 1100, 951, 762 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 7.39–7.22 (m, 5H, C_6H_5), 3.40–3.28 (m, 1H, PhCH), 2.77–2.60 (m, 4H, C(4) H_2 , C(6) H_2), 2.39 (s, 3H, COCH $_3$), 2.00 (s, 3H, C(3)CH $_3$); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 204.0, 196.4, 159.1, 142.4, 139.4, 128.8, 127.1, 126.5, 44.1, 40.1, 39.7, 31.7, 21.6. Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_2$: C, 78.92; H, 7.07%. Found: C, 78.92; H, 7.14%.

Ethyl 2-Hydroxy-3-(3-oxobutylidene)-1-cyclohexene-1-carboxylate (35). The reaction was performed as in the general procedure for **26** except that Michael acceptor **33** (51 μL , 0.50 mmol) was used, and dianion **34** was prepared by treatment of ethyl 2-oxocyclohexanecarboxylate (120 μL , 0.75 mmol) with 2 equiv of LDA in THF (3 mL) at -78°C for 5 min and at room temperature for 1 h.²⁴⁾ Compound **35** (58 mg, yield 50%) was obtained as a colorless oil. IR (neat) 2942, 1721, 1651, 1630, 1590, 1402, 1368, 1331, 1293, 1250, 1161, 1132, 1022, 812 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ = 6.60 (t, 1H, J = 9.0 Hz, C=CH), 4.23 (q, 2H, J = 7.1 Hz, OCH_2), 3.29 (d, 2H, J = 7.7 Hz, MeCOCH_2), 2.37–2.32 (m, 4H), 2.19 (s, 3H, COCH $_3$), 1.71–1.63 (m, 3H), 1.31 (t, 3H, J = 7.2 Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 205.3, 172.9, 164.0, 133.2, 122.4, 99.6, 60.5, 43.1, 29.7, 25.6, 22.9, 22.1, 14.2. Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_4$: C, 65.53; H, 7.61%. Found: C, 65.53; H, 7.68%.

Ethyl 2-Oxo-3-(3-oxobutyl)cyclohexanecarboxylate (36). The reaction was performed as in the general procedure for **26** except that α -silylated enone **19** (43 mg, 0.3 mmol) was used, and dianion **34** was prepared by treatment of ethyl 2-oxocyclohexanecarboxylate (72 μL , 0.45 mmol) with 2 equiv of LDA in THF (3 mL) at -78°C for 5 min and at room temperature for 1 h.²⁴⁾ Compound **36** (41 mg) was obtained as a colorless oil. IR (neat) 2940, 1717, 1647, 1615, 1371, 1302, 1258, 1105, 1026, 918, 837 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz), common values for both enol and keto forms: δ = 2.55 (t, 2H, J = 7.7 Hz, MeCOCH_2), 2.48–2.32 (m, 1H), 2.24–2.17 (m, 1H), 2.07–1.90 (m, 2H), 1.82–1.65 (m, 3H), 1.57–1.37 (m, 2H); enol form: δ = 12.44 (s, 1H, OH), 4.22 (q, 2H, J = 4.2 Hz, OCH_2), 2.17 (s, 3H, COCH $_3$), 1.32 (t, 3H, J = 4.2 Hz, OCH_2CH_3); keto form: δ = 4.22 (q, 2H, J = 4.2 Hz, OCH_2), 3.37 (m, 1H), 2.14 and 2.15 (s $\times$ 2, 3H, COCH $_3$), 1.31 (t, 3H, J = 4.2 Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , 75 MHz) δ = 208.8, 207.9, 207.3, 173.8, 172.9, 169.8, 98.0, 61.2, 60.8, 60.2, 57.9, 56.1, 49.9, 48.6, 41.3, 41.0, 40.9, 37.6, 34.6, 34.1, 30.8, 30.2, 29.8, 26.3, 24.0, 23.6, 23.4, 22.7, 21.7, 14.2, 14.1, 14.0. Anal. Calcd for $\text{C}_{13}\text{H}_{20}\text{O}_4$: C,

64.98; H, 8.39%. Found: C, 64.98; H, 8.54%.

(E)-3-Methyl-2-octen-4-one (37). Following the literature procedure,^{8b)} a 40% yield of **37** was obtained by treatment of (E)-2-methyl-2-butenic acid (3.0 g, 30 mmol) with 2.0 equiv of a hexane solution of *n*-BuLi (1.60 M; 37.5 mL) in ether (80 mL) at 0 °C for 30 min. IR (neat) 2959, 2874, 1669, 1646, 1456, 1379, 1227, 1120, 1071 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ = 6.74 (q, 1H, *J* = 6.9 Hz, CH), 2.64 (t, 2H, *J* = 7.3 Hz, COCH₂), 1.85 (d, 3H, *J* = 6.9 Hz, CHCH₃), 1.78 (s, 3H, CCH₃), 1.58 (quintet, 2H, *J* = 7.2 Hz, COCH₂CH₂), 1.34 (sextet, 2H, *J* = 7.2 Hz, CH₂Me), 0.91 (t, 3H, *J* = 7.2 Hz, CH₂CH₃); ¹³C NMR (CDCl₃, 75 MHz) δ = 202.1, 138.2, 136.8, 36.8, 27.1, 22.5, 14.7, 13.9, 11.0. Anal. Calcd for C₉H₁₆O: C, 77.09; H, 11.50%. Found: C, 77.05; H, 11.54%.

Methyl 5,6,6-Trimethyl-3,7-dioxoundecanoate (38). Following the general procedure for **26** except treatment with 5.0 equiv of MeOTf (0.57 mL, 5.0 mmol) after reacting dianion **25** of methyl acetoacetate (324 μ L, 3.0 mmol) with **37** (140 mg, 1.0 mmol), a 86% yield of Michael adduct **38** was obtained as a colorless oil. IR (neat) 2961, 2876, 1750, 1720, 1701, 1431, 1320, 1242, 1154, 1119, 1011 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ = 3.74 (s, 3H, OCH₃), 3.45 (s, 2H, COCH₂CO₂Me), 2.54–2.38 (m, 2H), 2.45 (t, 2H, *J* = 7.2 Hz, C(8)H₂), 2.29 (dd, 1H, *J* = 10.0, 16.9 Hz, C(4)HH), 1.52 (quintet, 2H, *J* = 7.2 Hz, C(9)H₂), 1.29 (sextet, 2H, *J* = 7.2 Hz, C(10)H₂), 1.05 (s, 3H, C(6)CH₃), 1.03 (s, 3H, C(6)CH₃), 0.90 (t, 3H, *J* = 7.2 Hz, C(11)H₃), 0.83 (d, 3H, *J* = 6.6 Hz, C(5)CH₃); ¹³C NMR (CDCl₃, 75 MHz) δ = 215.2, 201.8, 177.5(enol), 167.3, 90.1(enol), 52.1, 50.0, 49.1, 45.8, 36.5, 33.9, 25.9, 22.2, 21.2, 20.2, 14.9, 13.8. Anal. Calcd for C₁₅H₂₆O₄: C, 66.64; H, 9.69%. Found: C, 66.66; H, 9.87%.

Cyclization of Keto Ester 38 under Acidic or Basic Conditions. **Method A:** To a solution of **38** (16 mg, 0.06 mmol) in benzene (2.0 mL) was added a catalytic amount of *p*-TsOH at room temperature under argon. This reaction mixture was stirred under reflux condition for 1.5 h. The reaction was quenched with aqueous NaHCO₃, extracted with ether, dried, and concentrated. The residue was purified by column chromatography on silica gel (ether/hexane = 1/5 to 1/2 as the eluent) to give **40** (11.4 mg, yield 73%) as a colorless oil.

Method B To a solution of **38** (64 mg, 0.24 mmol) in MeOH (2.0 mL) was added MeONa (226 mg, 1.18 mmol) at room temperature under argon, and the mixture was refluxed for 0.5 h. The reaction was quenched with aqueous NH₄Cl, extracted with ether, dried, and concentrated. The residue was purified by column chromatography on silica gel (ether/hexane = 1/5 to 1/2 as the eluent) to give **39** (38 mg) and **40** (22 mg) (**39**:**40** = 37:63). Similarly, Bu₄NOH or RbOH was used to give **39** and **40** in ratios of 89:11 and 77:23, respectively.

Method C: To a solution of **38** (45 mg, 0.17 mmol) in CH₂Cl₂ (2.0 mL) was added a 1.0 M CH₂Cl₂ solution of TiCl₄ (0.84 mL, 0.84 mmol) at 0 °C under argon, and the mixture was stirred at 0 °C for 5 h. The reaction was quenched with 1 M HCl, extracted with ether, dried, and concentrated. The residue was purified by column chromatography on silica gel (ether/hexane = 1/5 to 1/2 as the eluent) to give **39** (43 mg, yield 100%) as a colorless oil.

Methyl 2-Butyl-3,3,4-trimethyl-6-oxo-1-cyclohexene-1-carboxylate (39). IR (neat) 2961, 2876, 1738, 1674, 1611, 1458, 1433, 1350, 1240, 1213, 1019 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ = 3.81 (s, 3H, OCH₃), 2.49 (dd, 1H, *J* = 17.3, 4.5 Hz, C(5)HH), 2.36–1.97 (m, 4H), 1.49 (quintet, 2H, *J* = 7.2 Hz, C(2)CH₂CH₂), 1.37 (sextet, 2H, *J* = 7.2 Hz, CH₂Me), 1.24 (s, 3H, C(3)CH₃Me), 1.09 (s, 3H, C(3)MeCH₃), 1.00 (d, 3H, *J* = 6.7 Hz, C(4)HCH₃), 0.91 (t, 3H, *J* = 7.2 Hz, CH₂CH₃); ¹³C NMR (CDCl₃, 75 MHz) δ = 194.9,

169.5, 167.8, 132.7, 61.8, 41.7, 39.4, 38.7, 31.7, 31.2, 25.2, 23.3, 20.4, 16.8, 13.4. Anal. Calcd for C₁₅H₂₄O₃: C, 71.39; H, 9.59%. Found: C, 71.19; H, 9.89%.

Methyl 4,4,5-Trimethyl-3-oxo-2-propyl-1-cyclohexene-1-acetate (40). IR (neat) 2963, 2874, 1742, 1669, 1638, 1458, 1435, 1329, 1259, 1171, 1109, 1021, 918, 733 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ = 3.71 (s, 3H, OCH₃), 3.26 (s, 2H, CH₂CO₂Me), 2.44–2.12 (m, 4H), 2.02–1.88 (m, 1H), 1.28 (sextet, 2H, *J* = 7.4 Hz, CH₂CH₃), 1.11 (s, 3H, C(4)MeCH₃), 0.96 (d, 3H, *J* = 6.8 Hz, C(5)HCH₃), 0.93 (s, 3H, C(4)CH₃Me), 0.88 (t, 3H, *J* = 7.4 Hz, CH₂CH₃); ¹³C NMR (CDCl₃, 75 MHz) δ = 204.0, 170.6, 145.6, 135.9, 52.1, 44.1, 39.6, 37.3, 36.6, 27.9, 22.6, 22.3, 18.2, 15.3, 14.1. Anal. Calcd for C₁₅H₂₄O₃: C, 71.39; H, 9.59%. Found: C, 71.41; H, 9.80%.

Methyl 3-Oxo-4-(3-oxocyclooctyl)butanoate (42). Using the general procedure outlined above for **26**, enone **8** (62 mg, 0.5 mmol) was combined successively with ATPH (1.0 mmol) and the dianion (**25**) of methyl acetoacetate (162 μ L, 1.5 mmol) to give **42** (83 mg, yield 70%). IR (neat) 2934, 1750, 1717, 1698, 1439, 1408, 1323, 1244, 1196, 1011 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ = 3.74 (s, 3H, OCH₃), 3.46 (s, 2H, CH₂CO₂Me), 2.76–2.12 (m, 7H), 1.98–1.77 (m, 2H), 1.76–1.55 (m, 2H), 1.55–1.16 (m, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ = 215.8, 201.4, 167.2, 90.4, 52.2, 49.1, 46.5, 42.3, 33.1, 31.8, 27.1, 25.3, 23.3. Anal. Calcd for C₁₃H₂₀O₄: C, 64.98; H, 8.39%. Found: C, 64.98; H, 8.45%.

Methyl 4-(cis-2-Methyl-3-oxocyclooctyl)-3-oxobutanoate (43). Using the general procedure outlined above for **26**, enone **41** (3.45 g, 25 mmol) was combined successively with ATPH (50 mmol) and the dianion (**25**) of methyl acetoacetate (8.09 mL, 75 mmol) to give **43** (4.76 g, yield 75%). IR (neat) 2936, 2860, 1748, 1715, 1698, 1653, 1628, 1446, 1323, 1240, 1101, 1011, 916, 733 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ = 3.75 (s, 3H, OCH₃), 3.48 (s, 2H, CH₂CO₂Me), 3.19 (m, 1H, CHMe), 2.90 (dt, 1H, *J* = 3.4, 11.8 Hz), 2.74 (dd, 1H, *J* = 6.6, 18.1 Hz, CHCHH(CO)), 2.53–2.36 (m, 1H), 2.49 (dd, 1H, *J* = 6.7 Hz, 18.0 Hz, CHCHH(CO)), 2.22 (m, 1H), 1.96 (m, 1H), 1.89–1.55 (m, 3H), 1.55–1.16 (m, 3H), 0.98 (d, 3H, *J* = 6.7 Hz, CHCH₃), 0.85 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ = 217.7, 201.8, 167.4, 90.6, 52.4, 49.5, 48.0, 47.3, 39.8, 31.5, 30.8, 29.3, 26.3, 23.7, 8.3. Anal. Calcd for C₁₄H₂₂O₄: C, 66.12; H, 8.72%. Found: C, 66.15; H, 8.61%.

Methyl 4-(2,2-Dimethyl-3-oxocyclooctyl)-3-oxobutanoate (46). Following the general procedure mentioned above for **26** except treatment with 5.0 equiv of MeOTf (28.3 mL, 250 mmol) after the reaction of the dianion (**25**) of methyl acetoacetate (150 mL, 150 mmol) with **37** (6.9 g, 50 mmol), a 89% yield of Michael adduct **46** was obtained as colorless solids. IR (neat) 2934, 1748, 1720, 1698, 1439, 1327, 1167, 756 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ = 3.76 (s, 3H, OCH₃), 3.49 (s, 2H, CH₂CO₂Me), 2.97 (m, 2H), 2.75 (dd, 1H, *J* = 3.0, 17.8 Hz, CHCHH(CO)), 2.33 (dd, 1H, *J* = 8.8 Hz, 17.8 Hz, CHCHH(CO)), 2.14 (dt, 1H, *J* = 3.8, 11.7 Hz), 1.98–1.55 (m, 4H), 1.47–1.23 (m, 3H), 0.99 (s, 3H, CCH₃Me), 0.95 (s, 3H, CMeCH₃), 0.88 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ = 219.6, 201.8, 167.3, 52.2, 49.4, 49.0, 44.0, 36.1, 34.8, 32.6, 20.6, 25.7, 24.8, 23.8, 15.6. Anal. Calcd for C₁₅H₂₄O₄: C, 67.14; H, 9.01%. Found: C, 67.24; H, 9.19%.

Methyl 9-Oxobicyclo[5.3.1]undec-7-ene-8-carboxylate (44). Using the Method C mentioned above for **38**, keto ester **42** (46 mg, 0.19 mmol) was treated with a 5.0 M CH₂Cl₂ solution of TiCl₄ (193 μ L, 0.96 mmol) in CH₂Cl₂ (3 mL) at ambient temperature for 3 h to give **44** (41 mg, yield 94%). IR (neat) 2926, 1731, 1666, 1628, 1431, 1371, 1334, 1224, 1078, 1003, 916, 753, 730 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ = 3.83 (s, 3H, OCH₃), 2.66 (dt, 1H,

$J = 3.1, 14.8$ Hz), 2.52 (dd, 1H, $J = 4.4, 27.1$ Hz), 2.45—2.17 (m, 5H), 2.13—1.65 (m, 5H), 1.43—0.96 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) $\delta = 195.3, 166.8, 164.2, 132.9, 51.8, 44.9, 33.7, 32.7, 32.1, 30.0, 28.4$ (two overlapped signals), 26.8. Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_3$: C, 70.24; H, 8.16%. Found: C, 70.24; H, 8.32%.

Methyl (1R, *11R*)-11-Methyl-9-oxobicyclo[5.3.1]undec-7-ene-8-carboxylate (45). Using the Method C mentioned above for **38**, keto ester **43** (254 mg, 1.0 mmol) was treated with a 5.0 M CH_2Cl_2 solution of TiCl_4 (1 mL, 5.0 mmol) in CH_2Cl_2 (20 mL) upon reflux for 2 h to give **45** (209 mg, yield 89%). IR (neat) 2922, 1734, 1668, 1628, 1450, 1333, 1250, 1210, 1084, 1043, 986 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) $\delta = 3.81$ (s, 3H, OCH_3), 2.88—2.68 (m, 2H), 2.54—2.31 (m, 2H), 2.17 (d, 1H, $J = 18.6$ Hz), 2.17—1.62 (m, 6H) 1.93—1.03 (m, 3H), 1.21 (d, 3H, $J = 6.9$ Hz, CHCH_3); ^{13}C NMR (CDCl_3 , 75 MHz) $\delta = 195.1, 169.7, 166.9, 131.7, 51.8, 39.1, 36.9, 35.7, 32.9, 32.6, 29.0, 28.4, 26.2, 18.9$. Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{O}_3$: C, 71.06; H, 8.53%. Found: C, 71.06; H, 8.62%.

Methyl 11,11-Dimethyl-9-oxobicyclo[5.3.1]undec-7-ene-8-carboxylate (47). To a 1,2-dichloroethane (4.0 mL) solution of keto ester **45** (54 mg, 0.20 mmol) was added a 5.0 M CH_2Cl_2 solution of TiCl_4 (1.2 mL, 6.0 mmol) over 12 h under reflux conditions. After the addition was completed, the mixture was stirred upon reflux for 3 h. Following the quenching and purification method outlined in the Method C, compound **47** (12.3 mg, yield 25%) was obtained. IR (neat) 2930, 2860, 1738, 1676, 1618, 1436, 1314, 1288, 1061, 826, 731 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) $\delta = 3.81$ (s, 3H, OCH_3), 2.76 (dd, 1H, $J = 5.2, 15.9$ Hz, $\text{C}(10)\text{-CHH}$), 2.33 (dd, 1H, $J = 3.9, 15.9$ Hz, $\text{C}(10)\text{CHH}$), 1.98 (m, 1H, $\text{C}(1)\text{H}$), 1.93—1.20 (m, 10H), 1.88 (s, 3H, $\text{C}(11)\text{MeCH}_3$), 1.27 (s, 3H, $\text{C}(11)\text{CH}_3\text{Me}$); ^{13}C NMR (CDCl_3 , 75 MHz) $\delta = 194.5, 167.6, 163.7, 132.5, 51.9, 45.2, 42.7, 42.1, 37.2, 29.7, 29.8, 27.9, 24.6, 21.2, 16.9$. Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_3$: C, 71.97; H, 8.86%. Found: C, 71.86; H, 8.91%.

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