The Diastereoselective Synthesis of Ester-Functionalized Alkenes through the Stereocontrolled Conjugate Addition (Michael Reaction) of Prochiral Enolates to Chiral α-Methylene β-Lactones and Thermal Decarboxylation of the Resulting α-Substituted β-Lactones

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The conjugate addition of ester and ketone enolates to α-methylene β-lactones **1** and **2** proceeds with high stereocontrol of the newly formed chiral centers. The β-lactones **3−8** with ester functionalities in the α-side chain were obtained in good yields from the addition of ester enolates, while the dispiro-β-lactones **9−11** were formed in the addition of acetophenone and propiophenone enolates. The decarboxylation of the resulting ester-functionalized β-lactones produced quantitatively the corresponding γ,δ-unsaturated esters **12−17** with complete retention of the initial β-lactone geometry. This unprecedented two-step sequence, i.e. Michael addition followed by decarboxylation, constitutes the first stereoselective synthesis of ester-functionalized, *(E)*-configurated alkenes, in which the synthetic potential of the α-methylene β-lactones as allene equivalents is advantageously utilized.

The ready availability of the highly functionalized α-methylene β-lactones by various methods[1] and their numerous reaction modes[2] as masked allenes[2,3] make these compounds attractive and valuable building blocks in organic synthesis. For example, their cycloaddition with dienes followed by stereoselective decarboxylation to the corresponding olefins with retention of the initial β-lactone geometry[4] has demonstrated that α-methylene β-lactones are useful allene equivalents. Moreover, the recent topological resolution by Diels−Alder cycloaddition and retrocleavage at moderate temperatures[5] provides convenient access to enantiomerically pure α-methylene β-lactones for asymmetric synthesis.

Recently, we have reported on the stereoselective synthesis of allyl amines and sulfides by nucleophilic addition of amines and thiols to α-methylene β-lactones and subsequent stereoselective (retention) decarboxylation of the resulting amino and thio β-lactones.[6] Since no general methods for the stereoselective preparation of γ,δ-unsaturated esters appear to have been reported, it was of interest to extend the conjugate addition methodology with α-methylene β-lactones to the Michael addition of ester enolates. Herein, we illustrate that the addition of ester enolates to α-methylene β-lactones and subsequent decarboxylation constitutes a general, stereocontrolled preparation of disubstituted γ,δ-unsaturated esters.

Results and Discussion

The lithium enolates were generated by treatment of the corresponding esters with lithium diisopropylamide (LDA) at −78 °C in tetrahydrofuran (THF) according to the method of Ireland.[7] The conjugate addition (Michael reaction) of the ester enolate of *tert*-butyl 2-methylpropionate to α-methylene β-lactones **2** at −78 °C afforded the mixture of the β-lactones *cis*-**3** and *trans*-**3** after hydrolysis with aqueous ammonium chloride (Scheme 1). The *cis:trans* ratio was 16:84, and as expected, the *trans* diastereoisomer is the thermodynamically favored product.[8] The decarboxylation of the mixture of the *cis*- and *trans*-β-lactones **3** afforded the mixture of γ,δ-unsaturated esters *(Z,E)*-**12** (Scheme 1). This sequence constitutes the first simple synthesis of such ester-functionalized alkenes from an α-methylene β-lactone as an allene equivalent. The *(Z,E)*-stereochemistry of the olefin is fixed by the *cis,trans* geometry of the β-lactones, since the decarboxylation proceeds diastereoselectively with retention of the configuration, as confirmed by control experiments.

When prochiral ester enolates were added to the α-methylene β-lactone **2**, the ester-functionalized β-lactones **4−8** (Scheme 2) were obtained after hydrolysis with aqueous NH_4Cl. The Michael addition proceeded in good yields (Table 1), and the observed *cis:trans* ratios ranged

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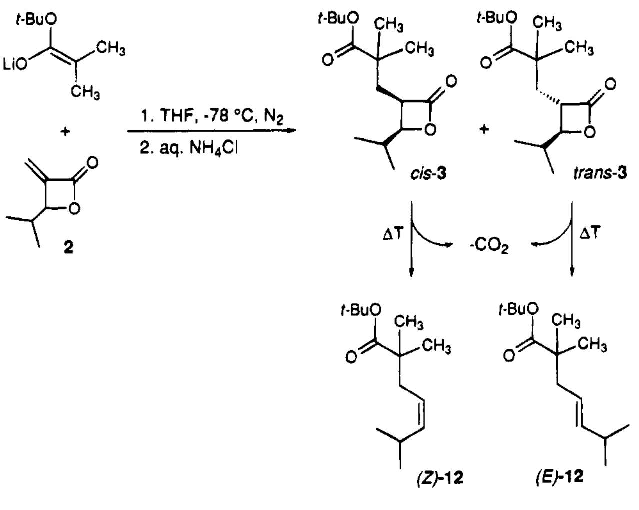
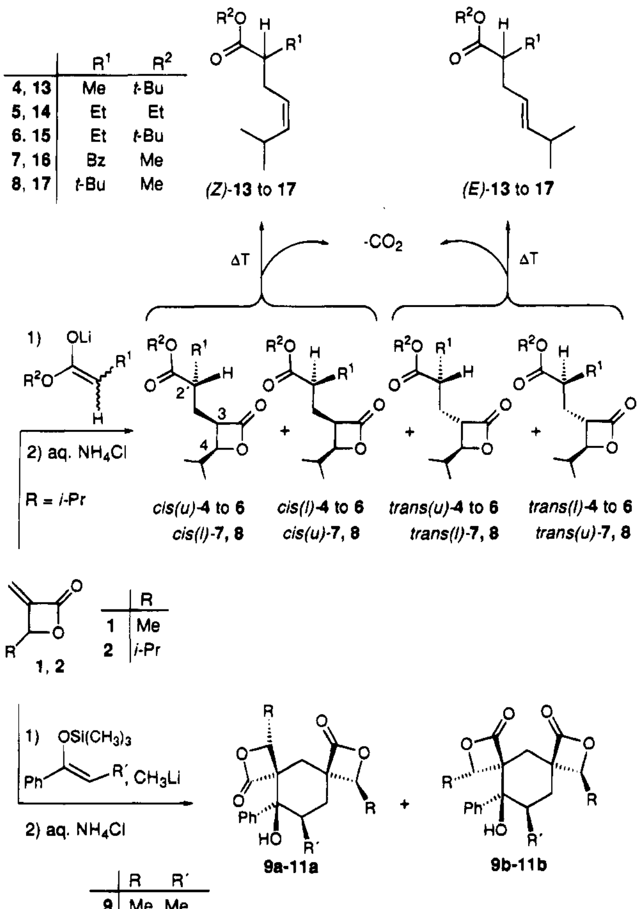
Scheme 1



Scheme 2



from 13:87 to 8:92 for the cases studied. The *cis,trans* stereochemistry of these ester-functionalized β-lactones was determined by the well-established empirical trends in the vicinal coupling constants (J_{cis} = ca. 6.5 Hz and J_{trans} = ca. 4.5 Hz)[9] for α,β-disubstituted β-lactones.

The relative configuration at the C-2′ position next to the ester functionality was assigned by chemical correlation for the *trans(u)*-**8** derivative (Scheme 3).

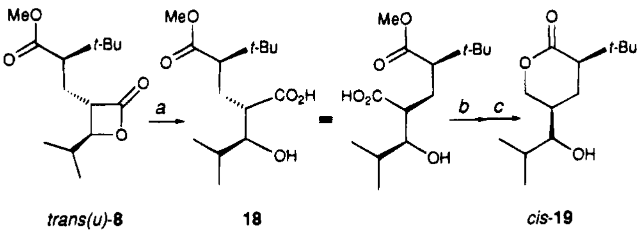
For convenience in retaining the *cis,trans* stereolabels, we use the Seebach–Prelog nomenclature,[10] where like (*l*) and unlike (*u*) refer to the C-4 position β to the lactone carbonyl group. First, the β-lactone *trans(u)*-**8** was saponified quantitatively to the hydroxy acid **18** (Scheme 3, step a). A control experiment confirmed that no deuteration took place at the C-3 position of the β-lactone and the C-2′ position of the side chain ester functionality under the hydrolysis conditions of the β-lactone *trans(u)*-**8** in deuterated methanol (CD_3OD), as monitored by ^{1}H NMR spectroscopy. Thus, epimerization of these stereogenic centers did not occur during the saponification. Reduction of the carboxylic acid group in the hydroxy acid **18** with diborane, followed by hydrolysis of the side chain ester group with NaOH in THF/H_2O at 68 °C, and finally acidification to pH 4 afforded exclusively *cis*-**19** (Scheme 3, steps b and c).

Table 1. Conjugate Nucleophilic Addition[a] (Michael Reaction) of Ester Enolates[b] to α-Methylene β-Lactone 2[c]

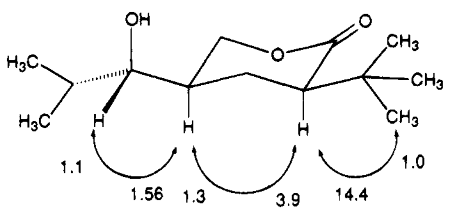
		diastereomeric ratios (dr)[d]				
		enolate[e]	product β-lactone			
entry	product	*Z*:*E* (%)	*cis*:*trans*[f]	*cis u*:*l*[g]	*trans u*:*l*[g]	yield[h] (%)
1	**4**	<5:95 (75)	11:89	<5:95	<5:95	63
2	**5**	18:82 (85)	13:87	<5:95	20:80	87
3	**6**	46:54 (94)	10:90	45:55	43:57	50
4	**7**	24:76 (99)	11:89	95:<5	77:23	88
5	**8**	<5:95 (97)	8:92	95:<5	95:<5	58

[a] Addition at −78 °C in THF and hydrolysis at −78 °C with NH_4Cl (aqueous) after 30 min. [b] Enolates were prepared by treatment of the corresponding esters with LDA. [c] For the structure code, see Scheme 2. [d] Determined by ^{1}H NMR analysis of the isolated material; relative yields normalized to 100%, error ca. 5% of the stated values, mass balance >95%. [e] In parentheses are given the yields of trimethylsilyl enol ether obtained after silylation of the corresponding lithium enolate. [f] Represents the sum of diastereomers *l* and *u* (*cis* adducts) versus *l* and *u* (*trans* adducts) for derivatives **4**–**8**. [g] Represents diastereoselectivities of the conjugate enolate addition at the stereogenic center α to the ester functionality. [h] Yield of isolated material after column chromatography.

Scheme 3



a) NaOH, 3:1 THF/H_2O, r.t., 10% HCl ; *b*) B_2H_6, THF, r.t., NH_4Cl (aqu.) ; *c*) NaOH, 3:1 THF/H_2O, 68 °C, 10% HCl.



NOE measurements (Scheme 3) proved unambiguously the *cis* configuration of the δ-lactone **19** and hence the *trans(u)* stereochemistry of the β-lactone **8**. The stereochemical assignments of the remaining β-lactones **4**–**7** were inferred by NMR spectral correlation with the known configuration of *trans(u)*-**8**. Thus, the *trans*

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diastereoisomers of β-lactones **4**–**8** have been shown to be the major products of this Michael addition (Table 1), i.e. the expected thermodynamically favored stereoisomer.[8]

For mechanistic elucidation of the stereochemical course in the Michael addition of the ester enolates to the α-methylene β-lactone **2**, the (*Z,E*)-geometry of the prochiral enolates was assessed by silylation (Table 1) with Me_3SiCl. For the *tert*-butyl propionate[11] and methyl 3,3-dimethylbutyrate,[12] the (*E*)-configurated ester enolates ($\geq$95%) were obtained exclusively on deprotonation of the corresponding esters with LDA in THF at −78 °C, as confirmed by ^1H NMR analysis (Table 1, entries 1 and 5).

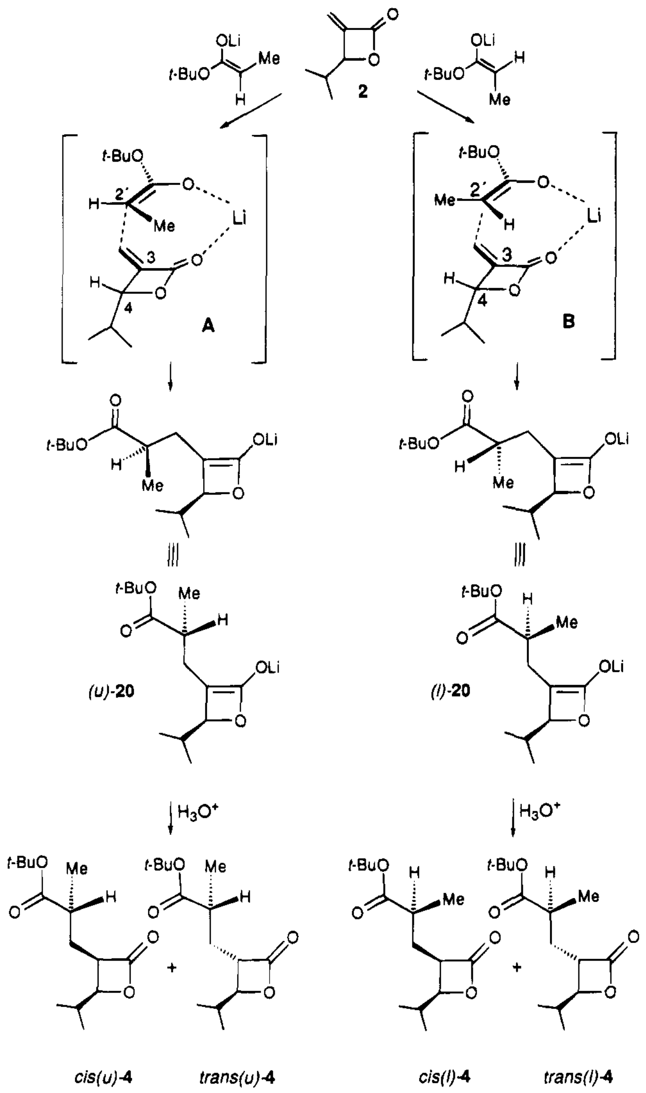
As shown by the stereochemical data in Table 1, the configurations of the Michael adducts reflect the initial ester enolate geometry. The configurational correspondence is excellent, except for the *cis(u)*-**5** and the *cis(l)*-**7** β-lactones (Table 1, entries 2 and 4). The latter are formed in such small amounts ($\leq$3% total) that presumably a rather large error precludes a sufficiently accurate determination of the dr values.

Illustrative and impressive examples are the (*E*)-enolates of *tert*-butyl propionate and methyl 3,3-dimethylbutyrate, which gave almost exclusively the *trans(l)*-**4** and *trans(u)*-**8** diastereomers (Table 1, entries 1 and 5). The (*E*)-enolates afforded the *cis(l)* and *trans(l)* adducts **4**–**6** and the *cis(u)* and *trans(u)* diastereoisomers **7** and **8** (note the substituent priority change), whereas the (*Z*)-enolates led to the *cis(u)* and *trans(u)* adducts **4**–**6** and the *cis(l)* and *trans(l)* diastereoisomers **7** and **8**. This establishes unequivocally the high stereoselectivity of these conjugate additions, provided the geometry of the prochiral ester enolate is controlled.

The mechanism in Scheme 4 attempts to rationalize the predominant formation of the *trans(l)* or the *trans(u)* diastereomer as a function of the enolate geometry. The conjugate addition step proceeds with efficient stereocontrol for the newly formed C-2′ chirality center relative to the already existing C-4 position in the β-lactone, as displayed by the transition states **A** and **B**. The practically complete (dr > 95%) diastereofacial stereocontrol in the Michael addition step derives from the planarity of the α-methylene β-lactone **2**, which for steric reasons is attacked from the ring face opposite the isopropyl group. Therefore, in the transition states **A** and **B**, a *trans* geometry applies. In analogy with other aldol reactions,[13] lithium ion coordination is the crucial π-facial-controlling feature for guaranteeing the essential restricted conformational geometry for high diastereoselectivity. In this context, we cite the so-called three-center diastereoselectivity[14] proposed for the aldol reaction of β-lactone enolates with aldehydes[14] and the Michael addition with dimethyl maleate.[15]

The stereochemistry of the incipient C-3 chirality center in the β-lactone is determined in the protonation step of the resulting β-lactone enolate **20** to the corresponding enol, which tautomerizes mainly to the *trans*-β-lactone diastereoisomer on thermodynamic grounds. So a high *trans:cis* diastereoselectivity is observed for protic electrophiles (NH_4Cl), but low temperatures (−78 °C) must be employed because the enolate decomposes above −50 °C.

Scheme 4



The low persistence at higher temperatures of the β-lactone enolate *(l)*-**20**, which is derived from the Michael addition of the enolate of *tert*-butyl propionate to the α-methylene β-lactone **2**, was established by trapping reactions with other electrophiles under the normal reaction conditions for the alkylation of β-lactone enolates (Scheme 5). Thus, nonstereoselective C-alkylation with methyl iodide and allyl bromide was observed in moderate yields (32–40%) at −60 °C to furnish the side chain, ester-functionalized β-lactones **21**. Moreover, above −50 °C, the acrylic acid **22** was detected in ca. 15% as a product of electrocyclic ring opening[16] of the β-lactone enolate *(l)*-**20**; the di-β-lactone **23** (ca. 5%) is the product of a second conjugate addition. The reaction of the enolate *(l)*-**20** with chlorotrimethylsilane at −30 °C led

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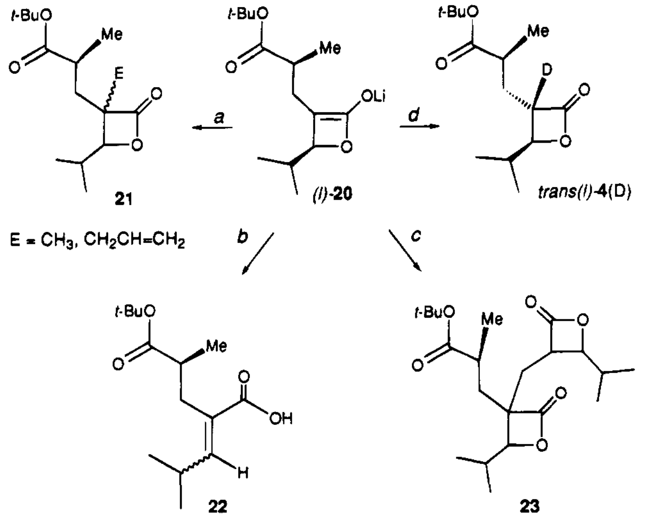
Scheme 5



[a] (a) CH_3I or $CH_2{=}CHCH_2Br$, −60 °C; (b) = (c) > −50 °C, NH_4Cl (aqueous); (d) D_2O, −78 °C.

Table 2. Conjugate Nucleophilic Addition[a] of Ketone Enolates[b] to α-Methylene β-Lactones 1 and 2[c]

entry	product lactone[c]	dr[d] of **a**:**b**	yield[e] (%)
1	**9**	75:25	59
2	**10**	60:40	65
3	**11**	69:31	46

[a] Addition at −50 °C in THF, warm up to 0 °C and hydrolysis with NH_4Cl (aqueous). [b] Enolates were prepared by treatment of the trimethylsilyl enol ether with CH_3Li. [c] For the structure code, see Scheme 2. [d] Determined by ^1H NMR analysis of the isolated material; relative yields normalized to 100%, error ca. 5% of stated values, mass balance 77–80%. [e] Yield of isolated material after column chromatography.

to a complex reaction mixture, as exhibited by ^1H and ^{13}C NMR analysis, which was not further characterized. Finally, exclusive deuteration at the C-3 position of the β-lactone moiety and none at the C-2′ chirality center of the ester side chain to afford *trans(l)*-**4**(D) excludes the transposition of the β-lactone enolate **20** to that of the ester enolate. Therefore, epimerization at the C-2′ position of the side chain is of no importance.

In contrast to the lithium ester enolates, the ketone enolates of propiophenone and acetophenone add to two molecules of the α-methylene β-lactones **1** and **2** to give the dispiro-β-lactones **9–11** (Scheme 2 and Table 2).

Thus, as expected,[18] these ketone enolates, which were generated from the silyl enol ethers[19] prepared according to the method of Stork[20] and House[21] (CH_3Li, 0 °C), are less reactive than the ester enolates. Consequently, the conjugate addition of the intermediary β-lactone enolate competes effectively. The (*Z*)-enolate of propiophenone afforded exclusively the stereochemically pure (dr > 95%) **9a,b** and **11a,b** diastereomers out of 16 possible ones. This also indicates that this Michael reaction proceeded with high π-facial stereocontrol of the new chirality centers (Scheme 2).

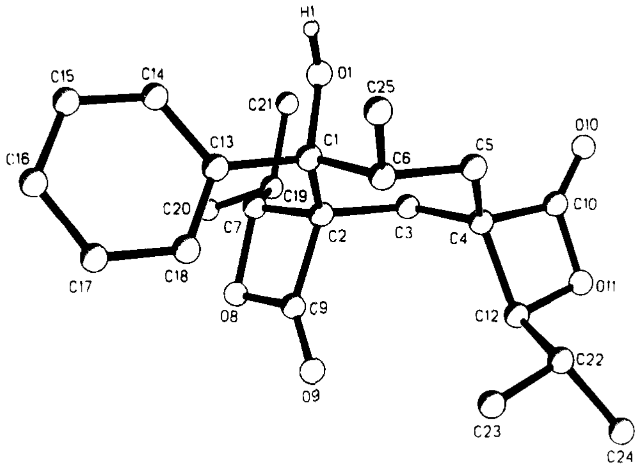


Figure 1. X-ray structure of the dispirolactone **11a**.

The configuration of dispirolactone **11a** was confirmed by X-ray analysis[22] (Figure 1), and the others were confirmed by NOE experiments. The diastereoselective attack of the enolate from the less hindered side of the α-methylene β-lactone **2** can be easily recognized from the stereochemistry of the hydroxy group (O-1 and H-1) and the β-lactone moiety (C-4, C-10, O-10, O-11, and C-12), which are on the same side. A transition state analogous to **A** seems to apply (Scheme 4), in which stereocontrol is exercised by lithium complexation between the O-1 and O-10 atoms during the conjugate addition of the first α-methylene β-lactone **2** to the ketone enolate.

The stereoselective (retention),[23] thermal decarboxylation of β-lactones has been known since the last century.[24] Thus, at moderate temperatures (below 200 °C),[9,23] a variety of substituted, functionalized alkenes have been obtained conveniently and efficiently by this procedure.[25] In the present application, the β-lactone *cis*-**3** gave exclusively the ester-functionalized alkene *(Z)*-**12** and correspondingly *trans*-**3** the diastereoisomer *(E)*-**12** (Scheme 1). Similarly, as shown in Scheme 2, the ester-functionalized β-lactones **4–8** were decarboxylated smoothly, when neat samples were heated at 180 °C to furnish the corresponding alkenes **13–17** in high yields (Table 3) and, as expected,[23] with complete retention of the initial β-lactone geometry. No isomerization of the olefin products was observed under the employed condi-

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[22] The colorless crystals of the dispirolactone **11a** were found to contain two molecules per unit cell: empirical formula, $C_{23}H_{30}O_5$ (386.4); crystal size, 0.4 × 0.75 × 0.3 mm³; space group, $P\bar{1}$; a = 1031.4(2) pm, b = 1135.4(2) pm, c = 906.8(2) pm, β = 92.23(1)°; V = 1059.8 × 10⁶ pm³; d = 1.211 g·cm⁻³; (Mo Kα) 4879 reflections collected, of which 3276 with $F > 3\sigma(F)$ were used in the solution of the structure; R = 0.059, R_w = 0.052. Detailed X-ray crystallographic data are available from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information GmbH, D-7514 Eggenstein-Leopoldshafen 2, upon quoting the depository number CSD-401348, the names of the authors, and the journal citation.

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Table 3. Decarboxylation[a] of the Ester β-Lactones[b] to γ,δ-Unsaturated Esters[b]

entry	product	diastereomeric ratios (dr)[c] β-lactone *cis:trans*	 olefin *Z:E*	yield[d] (%)
1	**13**	11:89	11:89	82
2	**14**	13:87	17:83	90
3	**15**	0:100	0:100	92
4	**16**	0:100	0:100	85
5	**17**	0:100	0:100	89

[a] Decarboxylation was run at 180 °C on the molten β-lactone. [b] For the structure code, see Scheme 1. [c] Determined by ^{1}H NMR analysis on the isolated material; mass balance > 95%, normalized to 100%, error ca. 5% of stated values. [d] Determined by ^{1}H NMR analysis of the crude product mixture with naphthalene as internal standard.

tions. For some cases, enriched as well as pure samples, prepared by chromatographic separation, of *trans*-β-lactone were used for decarboxylation (Table 3, entries 3–5). The olefinic products were purified by vacuum distillation (20 Torr) or silica gel chromatography. The vicinal *trans* coupling constant of ca. 15.5 Hz for the esters **12–17** establishes unequivocally the (*E*)-geometry of the double bond for the major olefin stereoisomer, which also confirms the *trans* stereochemistry of the respective β-lactones.

In conclusion, the present two-step sequence (Scheme 2), which utilizes the α-methylene β-lactones as allene equivalents,[2–6] constitutes the first stereoselective general synthesis of configurationally defined, ester-functionalized olefins by stereocontrolled (retention) decarboxylation of the corresponding β-lactones. The latter are now readily available by stereoselective conjugate addition of lithium ester enolates to the α-methylene β-lactones. Provided stereochemically pure enolates are employed, the *trans*-β-lactones have become accessible in high diastereoselective purity (≥89%). Therefore, the stereochemistry of the chirality center α to the ester group (the C-2′ position) in the side chain of the ester-functionalized β-lactones can also be dictated. Besides decarboxylation to complex olefins, the latter constitute highly functionalized and stereochemically defined building blocks for organic synthesis.

Experimental Section

General. All reactions were performed in oven-dried glassware under a positive pressure of argon or nitrogen. Air- and moisture-sensitive liquids and solutions were transferred by means of a syringe into the rubber septum-capped reaction vessels. Reaction mixtures and chromatography fractions were concentrated by using a rotary evaporator (ca. 20 °C/20 Torr). Elemental analyses were performed at the Analytical Division of the Institute of Inorganic Chemistry (University of Würzburg). For column chromatography, the Merck silica gel (230–400 mesh) was employed. Commercial grade reagents were used without further purification, except when indicated. THF was distilled from a sodium/benzophenone mixture immediately prior to use, diisopropylamine from CaH_2, and CH_2Cl_2 from P_2O_5. Petroleum ether was distilled from P_2O_5, and only the fraction with a bp of 30–50 °C was used for column chromatography.

General Procedure A for the Generation of Lithium Enolates from the Esters and Subsequent Conjugate Addition to α-Methylene β-Lactone 2. A 50-mL, two-necked, round-bottomed flask was equipped with an inlet adapter for argon or nitrogen gas and a rubber septum. It was charged with 20 mL of dry THF and diisopropylamine (1.00–4.35 mmol) and then cooled in an ice bath, and subsequently, a *n*-butyllithium solution (1.5 M in hexane, 1.1–4.35 mmol) was added rapidly by means of a syringe. After 15 min, the ice bath was replaced with a dry ice–acetone bath (−78 °C), a solution of the particular ester (0.79–2.38 mmol) in 1.0 mL of THF was added dropwise by means of a syringe over a period of 1 min, and the syringe was rinsed with THF (2 × 0.2 mL). After 30 min of stirring, a solution of α-methylene β-lactone **2**[1c] (0.39–2.38 mmol) in 1 mL of THF was added slowly over a period of 1 min. The resulting solution was stirred at −78 °C for 30 min and then treated with 20 mL of saturated, aqueous NH_4Cl solution. The resulting mixture was allowed to warm to room temperature, the aqueous phase was separated and extracted with two 30-mL portions of diethyl ether, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography on silica gel to yield the ester adducts **3–8** in 42–88% (Table 1). The yields, elemental analyses, and spectral data for the individual cases are described below.

***tert*-Butyl 2,2-Dimethyl-3-[2-(1-methylethyl)-4-oxo-3-oxetanyl]propionate (3).** According to the above general procedure A, from *tert*-butyl 2-methylpropionate (570 mg, 3.96 mmol), lithium diisopropylamide (4.35 mmol), and β-lactone **2** (250 mg, 1.98 mmol) was obtained 224 mg (42%) of a mixture of *cis*-**3** and *trans*-**3** after column chromatography [silica gel; petroleum ether/CH_2Cl_2 (1:9)] as a colorless oil. The *cis:trans* ratio was 16:84, as determined by NMR analysis of the characteristic β-lactone protons *cis*-H [δ 4.08 (dd)] and *trans*-H [δ 4.01 (dd)] directly on the crude product mixture: IR (CCl_4) 2960, 2920, 1810, 1730, 1460, 1380, 1360, 1135, 885, 845 cm^{-1}. Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.63; H, 9.69. Found: C, 66.39; H, 9.53. *cis*-**3**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.98 (d, *J* = 6.6 Hz, 3H), 1.02 (d, *J* = 6.4 Hz, 3H), 1.21 (s, 3H), 1.22 (s, 3H), 1.45 (s, 9H), 1.97 (oct, *J* = 6.7 Hz, 1H), 2.01 (d, *J* = 7.4 Hz, 2H), 3.61 (ddd, *J* = 4.2, 6.4, 9.1 Hz, 1H), 4.08 (dd, *J* = 6.5, 9.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 18.3 (q), 18.4 (q), 24.8 (q), 26.1 (q), 27.9 (q), 28.6 (d), 33.2 (t), 42.2 (s), 49.1 (d), 79.3 (s), 83.9 (d), 171.7 (s), 176.2 (s). *trans*-**3**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.99 (d, *J* = 6.7 Hz, 3H), 1.01 (d, *J* = 6.4 Hz, 3H), 1.19 (s, 3H), 1.21 (s, 3H), 1.43 (s, 9H), 1.97 (oct, *J* = 6.7 Hz, 1H), 2.01 (d, *J* = 7.4 Hz, 2H), 3.27 (dt, *J* = 4.1, 7.2 Hz, 1H), 4.01 (dd, *J* = 4.1, 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 17.1 (q), 17.6 (q), 24.7 (q), 26.5 (q), 27.9 (q), 31.9 (d), 38.3 (t), 42.1 (s), 50.8 (d), 80.6 (s), 82.9 (d), 171.3 (s), 176.1 (s).

***tert*-Butyl 2-Methyl-3-[2-(1-methylethyl)-4-oxo-3-oxetanyl]propionate (4).** According to the above general procedure A, from *tert*-butyl propionate (4.12 mg, 3.17 mmol), lithium diisopropylamide (3.48 mmol), and β-lactone **2** (200 mg, 1.58 mmol) was obtained 254 mg (63%) of a mixture of *cis(l)*-**4** and *trans(l)*-**4** as a colorless oil after column chromatography [silica gel; petroleum ether/CH_2Cl_2 (1:9)]. The *cis: trans* ratio was 11:89, as determined by NMR analysis of the characteristic β-lactone protons *cis*-H [δ 4.07 (dd)] and *trans*-H [δ 3.92 (dd)] directly on the crude product mixture: IR (CCl_4) 2975, 2955, 1810, 1730, 1450, 1380, 1360, 1145, 1100, 900, 880 cm^{-1}. Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.56; H, 9.44. Found: C, 65.84; H, 9.84. *cis(l)*-**4**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.91 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.39 (s, 9H), 1.60–2.23 (m, 3H), 2.65–2.80 (m, 1H), 3.60–3.75 (m, 1H), 4.07 (dd, *J* = 6.30, 10.48 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 17.7 (q), 17.9 (q), 28.0 (q), 28.7 (q), 31.9 (t), 32.2 (d), 38.0 (d), 51.9 (d), 79.9 (s), 80.7 (d), 170.9 (s), 174.6 (s). *trans(l)*-**4**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.90 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 1.11 (d, *J* = 7.1 Hz, 3H), 1.39 (s, 9H), 1.60–2.23 (m, 3H), 2.40–2.60 (m, 1H), 3.20–3.40 (m, 1H), 3.92 (dd, *J* = 3.98, 7.92 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 17.0 (q), 17.8 (q), 27.9 (q), 28.0 (q), 32.0 (t), 32.2 (d), 38.2 (d), 52.3 (d), 80.7 (s), 82.9 (d), 171.2 (s), 174.8 (s).

Ethyl 2-[[2-(1-Methylethyl)-4-oxo-3-oxetanyl]methyl]-butyrate (5). According to the above general procedure A, from ethyl butyrate (90.5 mg, 0.78 mmol), lithium diisopropylamide (1.03 mmol), and β-lactone **2** (50.0 mg, 0.39 mmol) was obtained 82 mg (87%) of a mixture of *cis(l)*-**5**, *trans(u)*-**5**, and *trans(l)*-**5** as a colorless oil after column chromatography [silica gel; petroleum ether/CH_2Cl_2 (1:9)]. The *cis:trans* ratio was 13:87, and the *trans(u)*-**5**:*trans(l)*-**5** ratio was 20:80, as determined by NMR analysis of the characteristic β-lactone protons *trans(u)*-**5**-H [δ 3.92 (dd)] and *trans(l)*-**5**-H [δ 3.90 (dd)] directly on the crude product mixture: IR (CCl_4) 2940, 2900, 1810, 1720, 1450, 1380, 1260, 1170, 1100, 880 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.43; H, 9.15. Found: C, 64.32; H, 9.10. *cis(l)*-**5**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.87–1.09 (m, 9H), 1.27 (t, J = 7.1 Hz, 3H), 1.45–2.66 (m, 6H), 3.61 (ddd, J = 4.6, 6.3, 12.3 Hz, 1H), 4.02–4.21 (m, 3H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.2 (q), 14.3 (q), 17.8 (q), 18.9 (q), 26.3 (t), 28.7 (d), 32.1 (t), 43.8 (d), 50.0 (d), 60.6 (t), 79.9 (d), 171.7 (s), 174.9 (s). *trans(u)*-**5**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.87–1.09 (m, 9H), 1.27 (t, J = 7.1 Hz, 3H), 1.45–2.84 (m, 6H), 3.18–3.25 (m, 1H), 3.92 (dd, J = 4.0, 8.0 Hz, 1H), 4.18 (t, J = 7.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.2 (q), 14.2 (q), 17.7 (q), 17.8 (q), 25.8 (t), 29.9 (d), 32.2 (t), 44.2 (d), 52.3 (d), 60.5 (t), 82.8 (d), 171.1 (s), 175.3 (s). *trans(l)*-**5**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.87–1.09 (m, 9H), 1.26 (t, J = 7.1 Hz, 3H), 1.45–2.66 (m, 6H), 3.26 (ddd, J = 3.9, 6.0, 9.7 Hz, 1H), 3.90 (dd, J = 4.0, 7.9 Hz, 1H), 4.18 (t, J = 7.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 11.3 (q), 14.3 (q), 16.9 (q), 17.8 (q), 25.5 (t), 30.0 (d), 32.1 (t), 44.4 (d), 51.9 (d), 60.6 (t), 83.0 (d), 170.7 (s), 174.6 (s).

***tert*-Butyl 2-[[2-(1-Methylethyl)-4-oxo-3-oxetanyl]-methyl]butyrate (6).** According to the above general procedure A, from *tert*-butyl butyrate (342 mg, 2.38 mmol), lithium diisopropylamide (3.08 mmol), and β-lactone **2** (150 mg, 1.19 mmol) was obtained 160 mg (50%) of a mixture of *cis(u)*-**6**, *cis(l)*-**6**, *trans(u)*-**6**, and *trans(l)*-**6** as a colorless oil after column chromatography [silica gel; petroleum ether/CH_2Cl_2 (1:9)]. The *cis:trans* ratio was 10:90, and the *cis(u)*-**6**:*cis(l)*-**6**, and *trans(u)*-**6**:*trans(l)*-**6** ratios were 45:55 and 43:57, respectively, as determined by NMR analysis of the characteristic β-lactone protons *cis(u)*-**6**-H [δ 4.13 (dd)], *cis(l)*-**6**-H [δ 4.11 (dd)], *trans(u)*-**6**-H [δ 3.93 (dd)], and *trans(l)*-**6**-H [δ 3.91 (dd)] directly on the crude product mixture: IR (CCl_4) 2950, 2920, 1815, 1730, 1460, 1380, 1360, 1150, 885, 845 cm^{-1}. Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.63; H, 9.69. Found: C, 66.48; H, 9.43. *cis(u)*-**6**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.90–1.10 (m, 9H), 1.46 (s, 9H), 1.52–2.55 (m, 6H), 3.55–3.74 (m, 1H), 4.13 (dd, J = 6.2, 9.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.0 (q), 17.3 (q), 18.9 (q), 26.0 (t), 27.8 (q), 29.7 (t), 31.3 (d), 44.7 (d), 50.1 (d), 80.1 (s), 84.2 (d), 171.8 (s), 174.7 (s). *cis(l)*-**6**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.90–1.10 (m, 9H), 1.46 (s, 9H), 1.52–2.55 (m, 6H), 3.55–3.74 (m, 1H), 4.11 (dd, J = 6.3, 10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.1 (q), 17.3 (q), 19.1 (q), 25.9 (t), 27.9 (q), 30.6 (t), 31.6 (d), 44.5 (d), 50.0 (d), 79.9 (s), 82.4 (d), 170.2 (s), 175.4 (s). *trans(u)*-**6**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.91 (t, J = 7.4 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.02 (d, J = 6.6 Hz, 3H), 1.47 (s, 9H), 1.52–2.55 (m, 6H), 3.15–3.32 (m, 1H), 3.93 (dd, J = 4.0, 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.1 (q), 17.0 (q), 17.7 (q), 25.9 (t), 28.0 (q), 30.1 (t), 32.2 (d), 45.1 (d), 52.3 (d), 80.7 (s), 82.8 (d), 171.2 (s), 174.2 (s). *trans(l)*-**6**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.92 (t, J = 7.5 Hz, 3H), 0.98 (d, J = 6.9 Hz, 3H), 1.03 (d, J = 6.6 Hz, 3H), 1.46 (s, 9H), 1.52–2.55 (m, 6H), 3.15–3.32 (m, 1H), 3.91 (dd, J = 3.9, 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.3 (q), 17.0 (q), 17.8 (q), 25.8 (t), 28.0 (q), 30.1 (t), 32.1 (d), 45.2 (d), 51.9 (d), 80.8 (s), 83.1 (d), 170.9 (s), 174.0 (s).

Methyl 2-(Phenylmethyl)-3-[2-(1-methylethyl)-4-oxo-3-oxetanyl]propionate (7). According to the above general procedure A, from methyl 3-phenylpropionate (781 mg, 4.76 mmol), lithium diisopropylamide (4.76 mmol), and β-lactone **2** (300 mg, 2.38 mmol) was obtained 604 mg (87%) of a mixture of *cis(u)*-**7**, *trans(l)*-**7**, and *trans(u)*-**7** as a colorless oil after column chromatography [silica gel; petroleum ether/CH_2Cl_2 (1:9)]. The *cis:trans* ratio was 11:89, and the *trans(l)*-**7**:*trans(u)*-**7** ratio was 77:23, as determined by NMR analysis of the characteristic β-lactone protons *cis(u)*-**7**-H [δ 4.08 (dd)], *trans(l)*-**7**-H [δ 3.89 (dd)], and *trans(u)*-**7**-H [δ 3.79 (dd)] directly on the crude product mixture: IR (CCl_4) 3080, 3040, 2970, 1840, 1745, 1610, 1450, 1170, 990, 700 cm^{-1}. Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.63. Found: C, 70.60; H, 7.55. *cis(u)*-**7**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.93 (d, J = 6.7 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H), 1.72–2.05 (m, 2H), 2.20–2.34 (m, 1H), 2.70–2.91 (m, 2H), 2.99–3.02 (m, 1H), 3.25 (ddd, J = 6.2, 6.4, 9.6 Hz, 1H), 3.66 (s, 3H), 4.08 (dd, J = 6.3, 10.4 Hz, 1H), 7.10–7.4 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 13.9 (q), 14.0 (q), 28.6 (d), 30.0 (t), 38.1 (t), 43.9 (d), 51.3 (q), 51.4 (d), 79.8 (d), 126.6 (d), 128.4 (2 d), 128.6 (2 d), 139.0 (s), 171.3 (s), 175.1 (s). *trans(l)*-**7**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.93 (d, J = 6.8 Hz, 3H), 1.01 (d, J = 6.6 Hz, 3H), 1.80–2.00 (m, 2H), 2.10–2.17 (m, 1H), 2.78 (dd, J = 10.0, 15.9 Hz, 1H), 2.94–3.09 (m, 2H), 3.23 (ddd, J = 3.9, 6.8, 9.5 Hz, 1H), 3.66 (s, 3H), 3.89 (dd, J = 4.0, 7.9 Hz, 1H), 7.10–7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 16.9 (q), 17.6 (q), 29.9 (t), 32.2 (d), 41.3 (t), 44.5 (d), 51.8 (q), 52.1 (d), 82.7 (d), 126.7 (d), 128.5 (2 d), 128.8 (2 d), 137.8 (s), 170.7 (s), 174.8 (s). *trans(u)*-**7**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.95 (d, J = 6.8 Hz, 3H), 1.02 (d, J = 6.6 Hz, 3H), 1.72–2.05 (m, 2H), 2.20–2.34 (m, 1H), 2.70–2.91 (m, 2H), 2.99–3.02 (m, 1H), 3.25 (ddd, J = 3.9, 6.4, 9.6 Hz, 1H), 3.68 (s, 3H), 3.79 (dd, J = 4.0, 7.8 Hz, 1H), 7.10–7.4 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 16.9 (q), 17.7 (q), 29.7 (t), 32.0 (d), 38.4 (t), 44.9 (d), 51.7 (q), 51.8 (d), 82.9 (d), 126.8 (d), 128.6 (2 d), 128.8 (2 d), 138.0 (s), 170.4 (s), 174.4 (s).

Methyl 3,3-Dimethyl-2-[[2-(1-methylethyl)-4-oxo-3-oxetanyl]methyl]butyrate (8). According to the above general procedure A, from methyl 3,3-dimethylbutyrate (514 mg, 3.96 mmol), lithium diisopropylamide (5.15 mmol), and β-lactone **2** (250 mg, 1.98 mmol) was obtained 286 mg (58%) of a mixture of *cis(u)*-**8** and *trans(u)*-**8** a as colorless oil after column chromatography [silica gel; petroleum ether/CH_2Cl_2 (1:9)]. The *cis:trans* ratio was 8:92, as determined by NMR analysis of the characteristic β-lactone protons *cis(u)*-**8**-H [δ 4.07 (dd)] and *trans(u)*-**8**-H [δ 3.87 (dd)] directly on the crude product mixture: IR (CCl_4) 2950, 2860, 1815, 1730, 1460, 1380, 1360, 1150, 1110, 885 cm^{-1}. Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.59; H, 9.43. Found: C, 65.60; H, 9.67. *cis(l)*-**8**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.91 (d, J = 6.7 Hz, 3H), 0.93 (s, 9H), 1.09 (d, J = 6.4 Hz, 3H), 1.76–2.36 (m, 4H), 3.38 (ddd, J = 4.7, 6.3, 12.6 Hz, 1H), 3.71 (s, 3H), 4.07 (dd, J = 6.3, 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 17.3 (q), 17.6 (q), 26.8 (t), 27.4 (q), 32.2 (d), 33.2 (s), 51.2 (q), 52.3 (d), 53.0 (d), 80.0 (d), 170.9 (s), 174.9 (s). *trans(u)*-**8**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.98 (d, J = 6.7 Hz, 3H), 0.99 (s, 9H), 1.05 (d, J = 6.6 Hz, 3H), 1.80–2.38 (m, 4H), 3.12 (dt, J = 4.3, 10.5 Hz, 1H), 3.72 (s, 3H), 3.87 (dd, J = 4.0, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 17.0 (q), 17.8 (q), 26.6 (t), 27.6 (q), 32.0 (d), 33.1 (s), 51.3 (q), 52.7 (d), 53.9 (d), 83.0 (d), 170.6 (s), 174.1 (s).

General Procedure B for the Generation of Lithium Enolates from the Ketone Silyl Enol Ethers and Subsequent Conjugate Addition to α-Methylene β-Lactones 1 and 2. A 50-mL, two-necked, round-bottomed flask was equipped with an inlet adapter for argon or nitrogen gas and a rubber septum. The flask was charged with 20 mL of dry THF and the particular silyl enol ether (0.79–6.34 mmol) and then cooled by means of an ice bath while the methyllithium solution (1.36 M in diethyl ether, 0.79–4.08 mmol) was added rapidly with a syringe. After 30 min, the ice bath was replaced with a dry ice–acetone bath (−78 °C), and a solution of the corresponding α-methylene β-lactone[1c] (0.39–3.17 mmol) in 1 mL of THF was added dropwise by means of a syringe over a period of 1 min and the syringe rinsed with THF (2 × 0.2 mL). The reaction mixture was allowed to warm to 0 °C over a period of 3 h, was treated with 20 mL of saturated, aqueous NH_4Cl solution, and was stirred for 15 min. The aqueous phase was separated and extracted with two 30-mL portions of diethyl ether, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography on silica gel to yield the dispirolactones **9**–**11** in 46–65% yields (Table 2). The yields, elemental analyses, and spectral data for the individual cases are described below.

Dispirolactone 9. According to the above general procedure B, from the trimethylsilyl enol ether of propiophenone (840 mg, 4.08 mmol), methyllithium (4.08 mmol), and β-lactone **1** (200 mg, 2.04 mmol) was obtained 140.4 mg of **9a** and 46.6 mg of **9b** (total yield 59% and dr = 60:40) as colorless amorphous solids after column chromatography (silica gel, CH_2Cl_2). **9a**: mp 149–151 °C; IR (CCl_4) 3620–3500, 3060, 3020, 2960, 1820, 1440, 1380, 1290, 1125, 900, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.97 (d, J = 6.7 Hz, 3H), 1.16 (d, J = 6.3 Hz, 3H), 1.61 (d, J = 6.3 Hz, 3H), 1.81 (d, J = 3.1 Hz, exchangeable with D_2O, 1H), 1.96 (dd, J = 12.6, 15.2 Hz, 1H), 2.13 (dd, J = 4.4, 15.2 Hz, 1H), 2.47 (s, 2H), 2.75 (dsext, J =

2.0, 6.7 Hz, 1H), 3.90 (dq, *J* = 3.2, 6.3 Hz, 1H), 4.70 (q, *J* = 6.3 Hz, 1H), 7.30–7.80 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 14.6 (q), 16.3 (q), 17.3 (q), 26.0 (t), 28.7 (t), 34.8 (d), 54.1 (s), 64.5 (s), 67.0 (d), 82.0 (d), 86.0 (s), 124.3 (d), 126.0 (d), 128.5 (d), 128.8 (d), 129.1 (d), 136.6 (s), 172.4 (s), 174.5 (s); MS (EI) *m/z* (relative intensity) 330 (M^+, 3.7), 105 (100). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.08; H, 6.71. Found: C, 68.85; H, 6.77. **9b**: mp 169–171 °C; IR (CCl_4) 3620–3500, 3060, 3020, 2960, 1820, 1440, 1380, 1290, 1125, 900, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.67 (d, *J* = 6.8 Hz, 3H), 1.38 (d, *J* = 6.4 Hz, 3H), 1.60 (br s, exchangeable with D_2O, 1H), 1.77 (d, *J* = 6.3 Hz, 3H), 1.91–2.12 (m, 2H), 2.28 (dd, *J* = 1.8, 13.8 Hz, 1H), 2.56 (d, *J* = 13.8 Hz, 1H), 2.58 (dsext, *J* = 2.4, 6.7 Hz, 1H), 4.40 (q, *J* = 6.5 Hz, 1H), 4.83 (q, *J* = 6.3 Hz, 1H), 7.24–7.70 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 15.0 (q), 15.1 (q), 15.6 (q), 28.3 (t), 29.2 (t), 33.4 (d), 56.1 (s), 63.9 (s), 73.8 (d), 79.1 (s), 81.0 (d), 125.9 (d), 126.2 (d), 128.2 (d), 128.6 (d), 129.1 (d), 140.1 (s), 171.9 (s), 173.8 (s); MS (EI) *m/z* (relative intensity) 330 (M^+, 2.3), 105 (100). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.08; H, 6.71. Found: C, 68.85; H, 6.74.

Dispirolactone 10. According to the above general procedure B, from trimethylsilyl enol ether of acetophenone (1.22 g, 6.34 mmol), methyllithium (6.34 mmol), and β-lactone **2** (0.400 g, 3.17 mmol) was obtained 216.0 mg of **10a** and 144.0 mg of **10b** (total yield 65% and dr = 60:40) as colorless squares after column chromatography (silica gel, CH_2Cl_2) and recrystallization from ethyl ether/*n*-pentane. **10a**: mp 156–158 °C; IR (CCl_4) 3590, 3040, 3000, 2940, 1820, 1460, 1260, 1150, 890, 710 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.76 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 1.07 (d, *J* = 6.5 Hz, 3H), 1.60 (br s, exchangeable with D_2O, 1H), 1.95–2.6 (m, 8H), 3.50 (dd, *J* = 2.1, 5.0 Hz, 1H), 4.00 (d, *J* = 9.6 Hz, 1H), 7.30–7.70 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 15.2 (q), 18.0 (q), 18.5 (t), 18.6 (q), 21.0 (q), 28.7 (d), 28.9 (d), 29.6 (t), 32.8 (t), 53.2 (s), 64.9 (s), 74.0 (d), 82.7 (s), 90.1 (d), 125.0 (d), 126.2 (d), 128.9 (d), 138.7 (s), 170.9 (s), 174.9 (s); MS (EI) *m/z* (relative intensity) 372 (M^+, 0.2), 254 (100). Anal. Calcd for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58. Found: C, 71.20; H, 7.84. **10b**: mp 148–150 °C; IR (CCl_4) 3590, 3060, 2940, 1820, 1460, 1260, 1140, 910, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.31 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.5 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.7 Hz, 3H), 1.60 (br s, exchangeable with D_2O, 1H), 1.93 (dsept, *J* = 1.8, 6.9 Hz, 1H), 2.1–2.6 (m, 7H), 4.00 (d, *J* = 0.6 Hz, 1H), 4.16 (d, *J* = 1.0 Hz, 1H), 7.30–7.70 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 18.2 (q), 18.6 (q), 18.6 (q), 19.4 (q), 22.0 (t), 27.7 (d), 29.0 (d), 30.2 (t), 34.5 (t), 55.8 (s), 64.6 (s), 72.9 (s), 81.8 (d), 89.6 (d), 126.2 (d), 128.5 (d), 128.7 (d), 142.4 (s), 171.8 (s), 174.9 (s); MS (EI) *m/z* (relative intensity) 372 (M^+, 0.1), 44 (100). Anal. Calcd for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58. Found: C, 71.24; H, 7.88.

Dispirolactone 11. According to the above general procedure B, from the trimethylsilyl enol ether of propiophenone (163.0 mg, 0.79 mmol), methyllithium (0.79 mmol), and β-lactone **2** (50.0 mg, 0.39 mmol) was obtained 48.3 mg of **11a** and 21.7 mg of **11b** (total yield 46% and dr = 69:31) after column chromatography (silica gel, CH_2Cl_2) and recrystallization from ethyl ether/*n*-pentane. **11a**: mp 164–166 °C, colorless needles; IR (CCl_4) 3590, 3060, 3020, 2960, 1820, 1460, 1150, 1130, 890, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.88 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H), 1.09 (d, *J* = 6.7 Hz, 3H), 1.15 (d, *J* = 6.6 Hz, 3H), 1.18 (d, *J* = 6.5 Hz, 3H), 1.3 (br s, exchangeable with D_2O, 1H), 1.95 (dsept, *J* = 1.8, 6.8 Hz, 1H), 2.02–2.21 (m, 3H), 2.42 (d, *J* = 15.7 Hz, 1H), 2.49 (d, *J* = 15.8 Hz, 1H), 2.63–2.8 (m, 1H), 3.58 (d, *J* = 1.8 Hz, 1H), 4.09 (d, *J* = 9.80 Hz, 1H), 7.30–7.80 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 14.8 (q), 15.1 (q), 18.0 (q), 18.6 (q), 21.1 (q), 26.7 (t), 28.7 (d), 28.9 (d), 29.4 (t), 35.6 (d), 53.7 (s), 65.4 (s), 74.2 (d), 85.2 (s), 90.3 (d), 124.4 (d), 126.1 (d), 128.3 (d), 128.8 (d), 129.0 (d), 137.5 (s), 171.1 (s), 174.9 (s); MS (EI) *m/z* (relative intensity) 386 (M^+, 3), 105 (100). Anal. Calcd for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.75; H, 8.14. **11b**: mp 162–164 °C, colorless squares; IR (CCl_4) 3640–3280, 3060, 2960, 1820, 1460, 1260, 1140, 910, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.68 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.31 (d, *J* = 6.8 Hz, 3H), 1.76 (br s, exchangeable with D_2O, 1H), 1.83–2.20 (m, 3H), 2.29–2.45 (m, 2H), 2.70–2.85 (m, 2H), 3.73 (d, *J* = 11.0 Hz, 1H), 4.46 (d, *J* = 5.78 Hz, 1H), 7.30–7.80 (m, 5H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 15.1 (q), 18.0 (q), 18.4 (q), 19.0 (q), 20.5 (q), 27.5 (d), 27.9 (t), 29.4 (d), 31.0 (t), 34.0 (d), 56.4 (s), 63.8 (s), 75.8 (s), 82.3 (d), 89.5 (d), 125.8 (d), 126.3 (d), 128.2 (d), 128.6 (d), 129.0 (d), 140.4 (s), 171.9 (s), 175.0 (s); MS (EI) *m/z* (relative intensity) 386 (M^+, 2), 44 (100). Anal. Calcd for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.68; H, 7.99.

General Procedure C for the Decarboxylation of the β-Lactones 3–8 to the γ,δ-Unsaturated Esters 12–17. The particular β-lactone (0.27–0.39 mmol) was placed into a round-bottomed flask, provided with a condenser and a bubble counter. The flask was heated in an oil bath at 180 °C and at atmospheric pressure until cessation of carbon dioxide evolution (ca. 5 min) and allowed to cool to room temperature. The γ,δ-usaturated esters **12–15** and **17** were purified by distillation at reduced pressure, while the derivative **16** was obtained by pure column chromatography (silica gel). The yields were determined by quantitative ^1H NMR analysis directly on the crude product mixture with naphthalene as internal standard and are given in Table 3. The physical constants, elemental analyses, and spectral data are described below for the individual cases.

***tert*-Butyl *(E)*-2,2,6-Trimethyl-4-heptenoate (12).** According to the above general procedure C, from β-lactone *trans*-**3** (100 mg, 0.370 mmol) was obtained 72.8 mg (87%) of olefin *(E)*-**12** as a colorless liquid (50 °C/20 Torr): IR (CCl_4) 3020, 2940, 2910, 1730, 1460, 1380, 1360, 1135, 900, 850 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.95 (d, *J* = 6.7 Hz, 6H), 1.10 (s, 6H), 1.42 (s, 9H), 2.16 (d, *J* = 6.7 Hz, 2H), 2.23 (oct, *J* = 6.7 Hz, 1H), 5.20–5.36 (m, 1H), 5.43 (dd, *J* = 5.9, 15.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 22.6 (q), 24.8 (q), 28.0 (q), 31.1 (d), 42.8 (s), 43.6 (t), 79.6 (s), 122.6 (d), 140.9 (d), 177.0 (s). Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.28; H, 11.57. Found: C, 74.34; H, 11.33.

***tert*-Butyl *(Z)*- and *(E)*-2,6-Dimethyl-4-heptenoate (13).** According to the above general procedure C, from a 11:89 mixture of *cis(l)*-**4**:*trans(l)*-**4** β-lactones (70.0 mg, 0.273 mmol) was obtained as a colorless liquid (50 °C/20 Torr) 47.5 mg (82%) of an 11:89 *Z*:*E* mixture of the olefin **13**. The *Z*/*E* ratio was determined by NMR analysis of the characteristic 6-methyl protons for the *(Z)*- [δ 0.93 (d)] and *(E)*- [δ 0.96 (d)] diastereoisomers directly on the crude product mixture: IR (CCl_4) 3020, 2960, 2930, 1730, 1460, 1370, 1150, 970, 850 cm^{-1}. Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.39; H, 11.13. *(Z)*-**13**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.93 (d, *J* = 6.6 Hz, 6H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.46 (s, 9H), 2.00–2.70 (m, 4H), 5.08–5.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 16.6 (q), 23.0 (q), 25.6 (d), 28.0 (q), 38.4 (t), 40.6 (d), 79.9 (s), 124.0 (d), 139.3 (d), 175.8 (s). *(E)*-**13**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.96 (d, *J* = 6.8 Hz, 6H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.45 (s, 9H), 2.00–2.70 (m, 4H), 5.08–5.31 (m, 1H), 5.43 (dd, *J* = 6.1, 15.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 16.6 (q), 22.5 (q), 28.1 (q), 31.0 (d), 36.8 (t), 40.6 (d), 79.8 (s), 123.8 (d), 139.8 (d), 175.7 (s).

Ethyl *(Z)*- and *(E)*-2-Ethyl-6-methyl-4-heptenoate (14). According to the above general procedure C, from a 13:27 mixture of *cis,trans*-**5** (100 mg, 0.413 mmol) was obtained 73.6 mg (90%) of a 17:83 (*Z*:*E*)-mixture of olefin **14** as a colorless liquid (50 °C/20 Torr). The *Z*:*E* ratio was determined by NMR analysis of the characteristic methylene alkoxy protons *(Z)* [δ 4.14 (q)] and *(E)* [δ 4.13 (q)] directly on the crude product mixture: IR (CCl_4) 3020, 2960, 2930, 1730, 1460, 1370, 1150, 970, 850 cm^{-1}. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.59; H, 11.16. *(Z)*-**14**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.83–1.00 (m, 9H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.40–1.75 (m, 2H), 2.01–2.70 (m, 4H), 4.14 (t, *J* = 7.1 Hz, 2H), 5.10–5.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.7 (q), 14.3 (q), 23.0 (q), 26.4 (t), 29.7 (d), 35.0 (t), 47.5 (d), 60.0 (t), 123.7 (d), 139.3 (d), 175.7 (s). *(E)*-**14**: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.83–1.00 (m, 9H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.40–1.75 (m, 2H), 2.01–2.41 (m, 4H), 4.13 (t, *J* = 7.1 Hz, 2H), 5.10–5.36 (m, 1H), 5.43 (dd, *J* = 6.2, 15.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.7 (q), 14.4 (q), 22.5 (q), 24.8 (t), 31.0 (d), 35.0 (t), 47.6 (d), 59.9 (t), 123.6 (d), 139.9 (d), 175.8 (s).

***tert*-Butyl *(E)*-6-Methyl-2-ethyl-4-heptenoate (15).** According to the above general procedure C, from a 43:57 mixture of *trans(u)*-**6** and *trans(l)*-**6** (100 mg, 0.370 mmol) was obtained 77.0 mg (92%) of (*E*)-**15** as a colorless liquid (50 °C/20 Torr): IR (CCl$_4$) 2980, 2870, 1730, 1460, 1380, 1360, 1150, 1120, 975, 855 cm^{-1}; ^{1}H NMR (CDCl$_3$, 250 MHz) δ 0.81–1.00 (m, 11H), 1.43 (s, 9H), 2.00–2.37 (m, 4H), 5.14–5.36 (m, 1H), 5.43 (dd, J = 5.9, 15.5 Hz, 1H); ^{13}C NMR (CDCl$_3$, 63 MHz) δ 11.7 (q), 22.5 (q), 25.3 (t), 28.2 (q), 31.0 (d), 35.2 (t), 48.4 (d), 79.8 (s), 124.0 (d), 139.5 (d), 175.1 (s). Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.28; H, 11.57. Found: C, 74.18; H, 11.77.

Methyl *(E)*-2-(Phenylmethyl)-6-methyl-4-heptenoate (16). According to the above general procedure C, from 90.0 mg (0.310 mmol) of a 23:77 mixture of *trans(l)*-**7** and *trans(u)*-**7** was obtained 65.0 mg (85%) of (*E*)-**16** as a colorless liquid, which was purified by flash chromatography [silica gel, petroleum ether/CH$_2$Cl$_2$ (3:1)]: IR (CCl$_4$) 3040, 3000, 2930, 2900, 1730, 1590, 1430, 1380, 1150, 960, 700 cm^{-1}; ^{1}H NMR (CDCl$_3$, 250 MHz) δ 0.88 (d, J = 6.7 Hz, 6H), 2.05–2.30 (m, 3H), 2.58–2.95 (m, 3H), 3.51 (s, 3H), 5.05–5.28 (m, 1H), 5.36 (dd, J = 6.5, 15.4 Hz, 1H), 7.03–7.24 (m, 5H); ^{13}C NMR (CDCl$_3$, 63 MHz) δ 22.5 (q), 31.0 (d), 34.9 (t), 37.6 (t), 47.8 (d), 51.3 (q), 123.1 (d), 126.2 (d), 128.3 (d), 128.8 (d), 139.3 (s), 140.6 (d), 175.8 (s). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.00; H, 9.00. Found: C, 78.00; H, 8.77.

Methyl *(E)*-6-Methyl-2-(1,1-dimethylethyl)-4-heptenoate (17). According to the above general procedure C, from *trans(u)*-**8** (100 mg, 0.390 mmol) was obtained 73.7 mg (89%) of olefin (*E*)-**17** as a colorless liquid (60 °C/20 Torr): IR (CCl$_4$) 3020, 2980, 2880, 1740, 1470, 1440, 1370, 1150, 975, 910 cm^{-1}; ^{1}H NMR (CDCl$_3$, 250 MHz) δ 0.86 (dd, J = 1.2, 6.7 Hz, 6H), 0.90 (s, 9H), 2.05–2.25 (m, 4H), 3.56 (s, 3H), 5.10–5.25 (m, 1H), 5.34 (dd, J = 6.5, 15.2 Hz, 1H); ^{13}C NMR (CDCl$_3$, 63 MHz) δ 22.5 (q), 27.8 (q), 30.8 (t), 31.0 (d), 32.9 (s), 50.6 (q), 56.8 (d), 124.4 (d), 139.7 (d), 175.2 (s). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.61; H, 11.72.

4-Carbomethoxy-5,5-dimethyl-2-(1-hydroxy-2-methylpropyl)hexanoic acid (18). A solution of β-lactone *trans(u)*-**8** (50.0 mg, 0.195 mmol) in 10 mL of THF and 3 mL of H$_2$O was stirred at room temperature, and then 3 mL of 0.071 M aqueous NaOH (0.213 mmol) was added. After 2 h, the reaction mixture was acidified to pH 2 with 10% aqueous HCl and extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over MgSO$_4$, and the solvent was removed (20 °C/20 Torr) to result quantitatively in the acid **18** as a pale yellow oil: IR (CCl$_4$) 3520, 3350–2450, 2960, 1735, 1700, 1470, 1370, 1150, 910, 650 cm^{-1}; ^{1}H NMR (CDCl$_3$, 250 MHz) δ 0.88 (d, J = 6.7 Hz, 3H), 0.95 (s, 9H), 0.97 (d, J = 6.6 Hz, 3H), 1.49–2.60 (m, 5H), 3.29 (dd, J = 3.3, 8.3 Hz, 1H), 3.64 (s, 3H), 6.5–7.1 (br s, exchangeable with D$_2$O, 2H); ^{13}C NMR (CDCl$_3$, 63 MHz) δ 18.9 (q), 19.3 (q), 27.4 (t), 27.6 (q), 32.5 (d), 33.2 (s), 45.7 (d), 51.1 (q), 53.4 (d), 76.0 (d), 175.2 (s), 180.2 (s). Anal. Calcd for $C_{14}H_{26}O_5$: C, 61.29; H, 9.55. Found: C, 61.55; H, 9.70.

***cis*-Tetrahydro-3-(1,1-dimethylethyl)-5-(1-hydroxy-2-methylpropyl)-2*H*-pyran-2-one (19).** A standard hydroboration apparatus^{26} was charged with acid **18** (100 mg, 0.365 mmol) in 10 mL of dry THF and BF$_3$·OEt$_2$ (46.8 mg, 0.400 mmol) in 5 mL of diglyme. NaBH$_4$ (13.7 mg, 0.300 mmol) in 5 mL of diglyme was added slowly to the trifluoroborate solution. After the cessation of diborane evolution, the THF solution was stirred for 12 h at room temperature. The reaction mixture was diluted with 20 mL of diethyl ether, 10 mL of saturated, aqueous NH$_4$Cl solution was added dropwise to destroy the excess of diborane, and the water phase was separated and extracted with diethyl ether (3 × 10 mL). The combined organic phases were dried over MgSO$_4$, the solvent was removed (20 °C/20 Torr), and the resulting oil was refluxed in a mixture of 10 mL of THF, 3 mL of H$_2$O, and 1.3 mL of a 0.427 M aqueous NaOH solution (0.547 mmol). After 2 h of refluxing, the reaction mixture was allowed to cool to room temperature, and it was diluted with diethyl ether (20 mL), acidified to pH 4 with 10% aqueous HCl, and stirred for 15 min. The water layer was separated and washed with diethyl ether (2 × 10 mL), and the combined ether extracts were dried over MgSO$_4$. On removal of the solvent (20 °C/20 Torr), an oil residue was obtained, which was purified by flash chromatography (silica gel, 1:1 diethyl ether/petroleum ether) to yield 45.0 mg (54%) of the *cis*-δ-lactone **19** as a colorless oil: IR (CCl$_4$) 3600, 3440, 2940, 1725, 1450, 1355, 1170, 900, 640 cm^{-1}; ^{1}H NMR (CDCl$_3$, 250 MHz) δ 0.90 (d, J = 6.7 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 1.08 (s, 9H), 1.35–2.40 (m, 6H), 3.28 (dd, J = 5.5, 6.0 Hz, 1H), 4.34 (d, J = 6.1 Hz, 2H); ^{13}C NMR (CDCl$_3$, 63 MHz) δ 15.2 (q), 19.9 (q), 24.9 (t), 27.5 (q), 29.5 (d), 33.1 (s), 36.5 (d), 48.7 (d), 68.6 (t), 76.4 (d), 173.2 (s). Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.10; H, 10.44.

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