Tandem Michael–Wittig–Horner Reaction: One-Pot Synthesis of δ-Substituted α,β-Unsaturated Carboxylic Acid Derivatives – Application to a Concise Synthesis of (*Z*)- and (*E*)-Ochtoden-1-al

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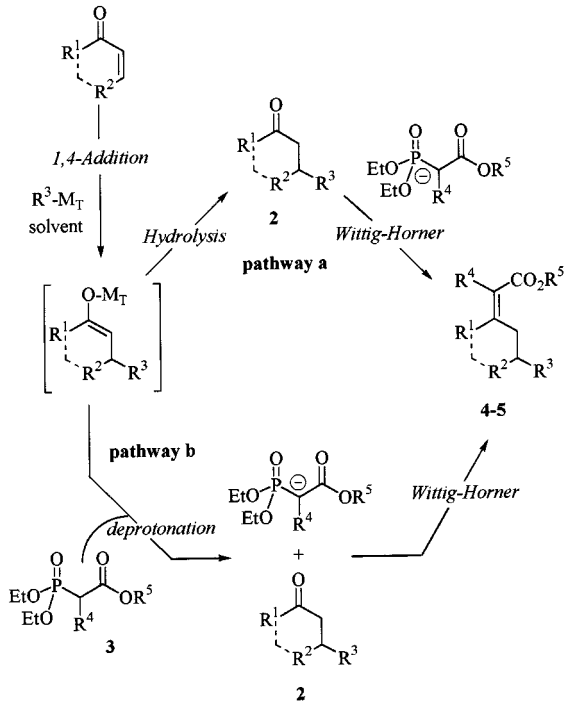
Keywords: Michael additions / Wittig reactions / Cuprates / Enones / Pheromones

A new tandem Michael–Wittig–Horner reaction has been developed to produce in high yields δ-substituted α,β-unsaturated esters, amides and lactones. The reaction has been successfully applied to a concise synthesis of (*E*)- and (*Z*)-ochtoden-1-als, components of the male sex pheromone of boll weevil from 3-methylcyclohex-2-en-1-one.

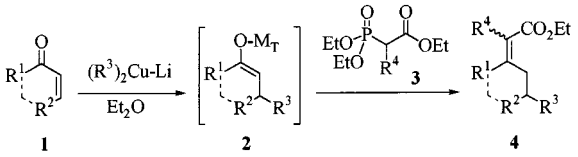
Introduction

Tandem reactions have recently emerged as promising and successful procedures for the preparation in only one step of highly functionalized compounds.[1,2] In connection with our work on asymmetric isomerization reactions,[3] we were recently interested in preparing δ-substituted α,β-unsaturated esters **4**–**5**. 1,4-Additions of organometallic reagents[4] to alkenals or enones **1** followed by a Wittig–Horner process[5] appeared to be one of the best ways to achieve this goal (Scheme 1 – pathway a).



Scheme 1

We considered performing this sequence in only one step using a new tandem process according to Scheme 1 – pathway b. The copper enolate produced after the initial 1,4-addition was presumed to be able to deprotonate the phosphonoester, which possesses at least one highly acidic proton in the α-position. Hence, both the carbonyl group and the anion of the phosphonoester should be generated. Coupling between these two species could then deliver the desired α,β-unsaturated ester. This strategy should avoid the isolation of the ketone/aldehyde **2**, which could in some cases exhibit a significantly low boiling point or high volatility. Therefore, better yields could be attempted (Scheme 2).



Scheme 2

We wish to report here results obtained from various ketones and aldehydes, different nucleophilic species (organocopper and -lithium compounds), and also different phosphono derivatives.[6] The reaction was first tested on cycloalkenones in the presence of cuprates easily prepared according to literature procedures. Results are summarized in Table 1.

According to these results, the reaction occurred and gave adducts in good to excellent yields even with cycloalkenones substituted at the 3-position. It should be pointed out that the one-pot procedure, avoiding the purification of compounds **2**, delivered the esters **4** with the same efficiency as the two-step process, as shown for the synthesis of **4d** (Scheme 3).

Furthermore, in the case of the highly substituted phosphonate **3b** (R^4 = Me), exclusive formation of the α,β-unsaturated ester **4d** was observed without isomerization to the β,γ-unsaturated isomer **4d′** during the tandem process; this contrasts with previously reported double-bond migra-

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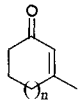
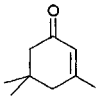
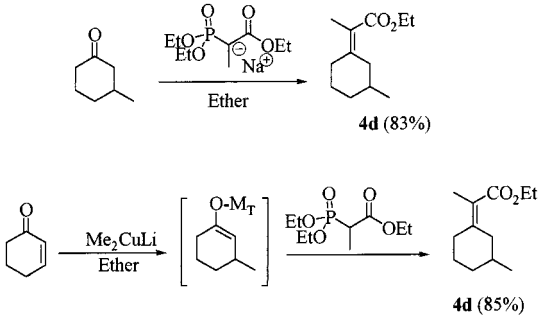
Table 1. Tandem Michael−Wittig−Horner addition on cycloalkenones

Entry	Substrate	n	Nucleophile $(R^3)_2Cu$-Li	Phosphonate 3 R^4	Adduct 4	Yield	E / Z
1		0	Me_2CuLi	H	**4a**	68% [a]	52 / 48
2		0	$(Bu)_2CuLi$	H	**4b**	89% [a]	50 / 50
3		1	Me_2CuLi	H	**4c**	84% [a]	50 / 50
4		1	Me_2CuLi	H	**4c**	70% [b]	50 / 50
5		1	Me_2CuLi	H	**4c**	68% [c]	50 / 50
6		1	Me_2CuLi	Me	**4d**	85% [a]	50 / 50
7		1	$(Bu)_2CuLi$	H	**4e**	93% [a]	50 / 50
8		1	Ph_2CuLi	H	**4f**	96% [a]	50 / 50
9		1	Ph_2CuLi	H	**4f**	56% [c]	50 / 50
10		0	Me_2CuLi	H	**4g**	82% [a]	52 / 48
11		1	Me_2CuLi	H	**4h**	83% [a]	77 / 23
12		1	Me_2CuLi	H	**4i**	83% [a]	-

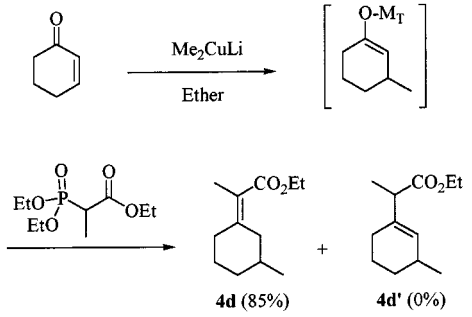
[a] Quenching of the enolate performed with phosphonate **3** (2 equiv.). − [b] Quenching of the enolate performed with a mixture of ammonium chloride (0.9 equiv.) and phosphonate **3** (1.2 equiv.). − [c] Quenching of the enolate performed with a mixture of acetic acid (0.9 equiv.) and phosphonate **3** (1.2 equiv.).



Scheme 3

tion during Wittig−Horner reactions involving cyclic enones and such hindered phosphonoesters (Scheme 4).[7]

A major drawback of our method is the lack of *E*/*Z* selectivity. This results from low discrimination between the

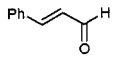
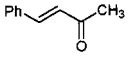
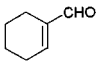
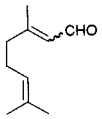


Scheme 4

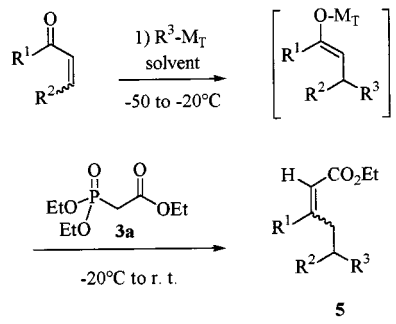
two stereotopic faces of ketone **2** by the phosphonoester anion, because of the large distance between the electrophilic center and the substituted C-3 position. This problem therefore appears difficult to overcome. Moreover, the reaction was initially performed with 2 equivalents of phosphonoester **3**, one to quench the copper enolate and one to neutralize the second anion species. In order to reduce this quantity, we introduced only one equivalent of **3** in association with one equivalent of another acidic compound such as acetic acid or ammonium chloride. The reaction still appeared efficient while the yields were slightly reduced (Entries 1b and 1c).

The reaction was also tested on acyclic enones and unsaturated aldehydes as reported in Table 2.

Table 2. Tandem Michael−Wittig−Horner reaction on acyclic enones and unsaturated aldehydes

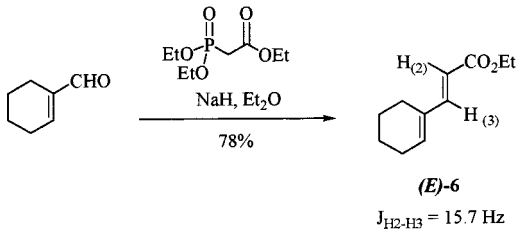
Entry	Substrate	Nucleophile	Conditions	3a (equiv.)	Adduct 5	yield	E / Z
1		Me_2CuLi	Et_2O, -50°C	2	**5a**	15%	100/0
2		$Me_5Cu_3Li_2$	Et_2O, -50°C	5	**5a**	47%	100/0
3		Me_2CuLi	Et_2O, -50°C	2	**5b**	34%	not det.
4		$Me_5Cu_3Li_2$	Et_2O, -50°C	5	**5b**	72%	87/13
5		Me_2CuLi	Et_2O, -50°C	2	**5c**	65%	100/0[a]
6		Me_2CuLi	Et_2O, -50°C	2	**5d**	81%	100/0
7		DIBAL	THF/HMPA -50°C	1	**5e**	41%	50/50

[a] 32:68 ratio of *cis* and *trans* stereoisomers of pure (*E*)-**5c**.



Scheme 5

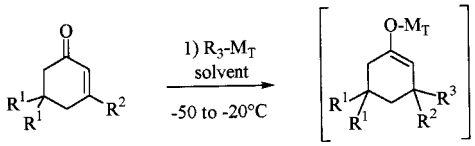
Using dimethylcuprates, the reaction took place but appeared less selective (1,2- versus 1,4-addition). To suppress this side-reaction, the use of higher order organocuprates as recommended by Clive[8] and Lipshutz[9] was followed. As claimed, the yields were significantly increased (Entries 2 versus 1 and 4 versus 3). Furthermore, using a procedure first described by Tsuda et al.,[10] we were also able firstly to reduce the C=C double bond of the enone by conjugate addition of a hydride species before performing the

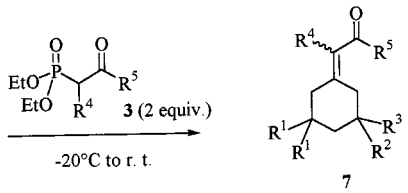


Scheme 6

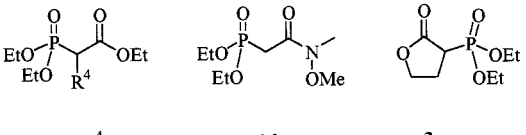
Wittig–Horner reaction. In this case, the overall yield appeared less significant than expected. Moreover, the *E*/*Z* selectivity was poor compared to the addition of methylcuprate on similar substrates, which preferentially delivered the *E* isomer. It should be noted that compound **5c** was obtained as a mixture of two compounds identified as a *syn*/*anti* mixture. The determination of the *E* geometry of the new double bond was established from the coupling constant measured between the two olefinic protons (J = 15.7 Hz) and confirmed by synthesizing ester **6**, which exhibits the same coupling value (Scheme 6).

The reaction was also conducted using various functionalized nucleophiles or different phosphonocarboxylic derivatives **3** with cyclohexenone and 3-methylcyclohexenone (Scheme 7,8 and Table 3).





Scheme 7



3a (R^4=H) **3d** **3e**
3b (R^4=Me)
3c (R^4=F)

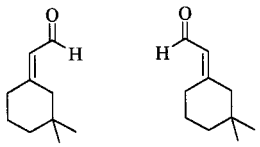
Scheme 8

For example, 1,4-addition of the anion of 1,3-dithiane (Entry 1) or dimethyl malonate (Entry 2) was selectively achieved in the presence of HMPA.[11] After quenching with an excess of phosphonate **3a**, adducts **7a** and **7b** were obtained in 78 and 92% yields, respectively. For the reaction of nitromethane (Entry 4) and cyclohex-2-en-1-one carried out in the presence of basic alumina,[12] we observed only 3-nitromethylcyclohexanone, resulting from the 1,4-addition process. In this case, phosphonate **3a** is probably deprotonated in situ by the solid base present in large excess, preventing the indispensable concomitant neutralisation of the 3-nitromethylcyclohexanone enolate.

Table 3. Tandem Michael–Wittig–Horner reaction with functionalized nucleophiles

Entry	Substrate R^1	Substrate R^2	Nucleophile R^3-H conditions	Phosphonate 3 R^4	Phosphonate 3 R^5	Adduct 7	Adduct 7 yield	Adduct 7 (E/Z)
1	H	H	1,3-dithiane, n-BuLi, THF HMPA	**3a** H	Et	**7a**	78%	(55/45)
2	H	H	Dimethylmalonate *n*-BuLi, THF HMPA	**3a** H	Et	**7b**	92%	(60/40)
3	Me	Me	Me_2CuLi ether	**3c** F	Et	**7c**	64%	(-)
4	H	H	CH_3-NO_2 Al_2O_3 neat	**3a** H	Et		0% [a]	
5	H	H	Me_2CuLi ether	**3d** H	N(Me)OMe	**7d**	82%	(52/48)
6	H	H	Me_2CuLi ether	**3e** -CH_2-CH_2-		**7e**	97%	(-)

[a] 3-Nitromethylcyclohexanone was the main product isolated under these conditions.



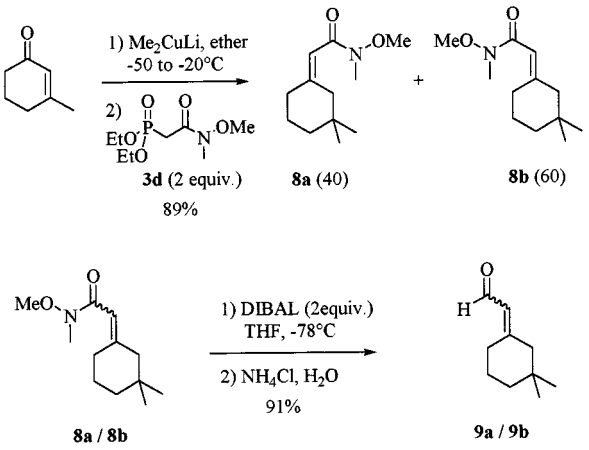
9a **9b**

Scheme 9

Finally, we conducted an application of this tandem Michael–Wittig–Horner reaction to the synthesis of (*Z*)- and (*E*)-2-ochtoden-1-als (**9a** and **9b**), components of the male sex pheromone of the boll weevil *Anthonomus grandis*[13] (Scheme 9). While these compounds have in many cases already been prepared by different groups, the previous syntheses needed numerous steps.[14]

3-Methyl-2-cyclohex-1-one was submitted to conjugate addition of lithium dimethylcuprate. The intermediate enolate was quenched with the commercially available phosphonoacetamide **3d**, thus leading to 3,3-dimethylcyclohexanone and the stabilized ylide of **3d**. Subsequent Wittig–Horner reaction took place between these two species giving in high yield a mixture of *E* and *Z* unsaturated Weinreb[15] amides **8a** and **8b** (Scheme 10), which were partially separated by carefully conducted flash chromatography.

A mixture of amides **8a** and **8b** was then submitted to reduction with DIBAL (2 equivalents) according to published procedures,[15] and furnished compounds **9a** and **9b** in good yields. Pure **8b** underwent reduction under the same conditions and gave **9b** as sole product in comparable yield (90%). Comparison between the NMR spectra of **9b** and data in the literature[14] allowed attribution of the *E* and *Z* configurations to **8b** and **8a**, respectively.



Scheme 10

In conclusion, we have designed a new procedure for the preparation in one step of highly functionalized δ-substituted α,β-unsaturated carboxylic derivatives in high yield. The synthesis of (*Z*)- and (*E*)-2-ochtoden-1-als, performed in a straightforward manner, represents the first application of this tandem Michael−Wittig−Horner reaction.

Experimental Section

General: Solvents and commercially available reagents were purified according to standard procedures.[16] − TLC control was performed using silica-gel plates 60 F_{254} from Merck. Compounds were purified by flash chromatography[17] using 43−60 mesh Merck silica. − ^{1}H NMR and ^{13}C NMR spectra were obtained with a Bruker AC 250 (^{1}H NMR: 250 MHz, ^{13}C NMR: 63 MHz) spectrometer, in $CDCl_3$ and with TMS as internal standard. − IR spectra were measured with an FT-IR MIRDAC spectrometer. − Mass spectra were recorded at the Faculty of Pharmacy of Reims with a JEOL D-300 apparatus at 70 eV.

General Procedures. − Procedure A: In a two-necked flask, dried prior to use, was placed copper iodide (0.43 g, 2.25 mmol) in diethyl ether (25 mL). The solution was cooled to 0 °C and a solution of methyllithium in hexane (1.6 M, 2.8 mL, 4.50 mmol) was carefully added. After 20 min at this temperature, the milky solution was cooled to −78 °C and the enone/aldehyde (2.25 mmol) was added dropwise. The resulting dark yellow mixture was stirred for 2.5 h while the temperature reached −15 °C. Phosphonate **3** (4.50 mmol), dissolved in diethyl ether (1 mL), was added. The solution was stirred overnight, then hydrolyzed with a saturated solution of ammonium chloride (25 mL). The crude solution was extracted with diethyl ether (3 × 25 mL), dried with $MgSO_4$, filtered and concentrated. The pure compound was obtained as a mixture of *E* and *Z* isomers after flash chromatography on silica (eluent: hexanes/ethyl acetate, 93:7).

Procedure B: Same procedure as procedure A but using 3 equivalents of copper iodide and 5 equivalents of methyllithium.

Ethyl (3-Methylcyclopentylidene)acetate (4a):[18] Prepared according to Procedure A using cyclopentenone and phosphonate **3a** as substrates. Liquid (0.26 g, 68%); *E*/*Z* = 52:48. − IR (neat): $\tilde{\nu}$ = 2950, 2870, 1715, 1655, 1465, 1370, 1205 cm^{-1}. − ^{1}H NMR ($CDCl_3$): *E* isomer: δ = 1.05 (d, 3 H, *J* = 6.5 Hz), 1.27 (t, 3 H, *J* = 7.2 Hz), 1.70−2.75 (m, 6 H), 3.09 (dd, 1 H, *J* = 7.2 and 18.7 Hz), 4.14 (q, 2 H, *J* = 7.2 Hz), 5.75 (s, 1 H). − *Z* isomer: δ = 1.01 (d, 3 H, *J* = 6.1 Hz), 1.26 (t, 3 H, *J* = 7.2 Hz), 1.70−2.75 (m, 6 H), 2.96 (dd, 1 H, *J* = 7.2 and 18.7 Hz), 4.14 (q, 2 H, *J* = 7.2 Hz), 5.75 (s, 1 H). − ^{13}C NMR ($CDCl_3$): *E* isomer: δ = 14.3 (q), 19.7 (q), 33.4 (t), 34.3 (d), 35.2 (t), 44.1 (t), 59.3 (t), 111.8 (d), 166.8 (s), 168.8 (s). − *Z* isomer: δ = 14.3 (q), 19.3 (q), 32.1 (t), 33.6 (t), 34.7 (d), 44.1 (t), 59.3 (t), 111.7 (d), 166.8 (s), 168.9 (s).

Ethyl (3-Butylcyclopentylidene)acetate (4b): Prepared according to Procedure A using cyclopentenone and phosphonate **3a** as substrates and *n*-butyllithium instead of methyllithium. Liquid (0.42 g, 89%); *E*/*Z* = 52:48. − IR ($CHCl_3$): $\tilde{\nu}$ = 2956, 2888, 1715, 1655, 1460, 1370, 1200, 1125 cm^{-1}. − ^{1}H NMR ($CDCl_3$): Mixture of *E* + *Z* isomers: δ = 0.89 (t, 3 H, *J* = 6.9 Hz), 1.27 (t, 3 H, *J* = 7.2 Hz), 1.15−1.45 (m, 7 H), 1.86−1.95 (m, 2 H), 2.04 (ddt, 0.5 H, *J* = 17.0 Hz, 7.2 Hz and 1.4 Hz), 2.21 (ddt, 0.5 H, *J* = 17.0 Hz, 7.1 Hz and 1.3 Hz), 2.34−2.69 (m, 2 H), 2.97 (dd, 0.5 H, *J* = 18.0 Hz and 7.2 Hz) and 3.13 (dd, 0.5 H, *J* = 19 Hz and 7.2 Hz), 4.15 (q, 1 H, *J* = 7.2 Hz), 4.16 (q, 1 H, *J* = 7.2 Hz), 5.75 (s, 1 H). − ^{13}C NMR ($CDCl_3$): *E* + *Z* isomers: δ = 14.0 (q), 14.3 (q), 22.8 (t), 30.5 (t), 30.6 (t), 31.6 (t), 321 (t), 32.4 (t), 34.5 (t), 35.0 (t), 35.2 (t), 39.2 (d), 40.3 (d), 39.3 (t), 42.5 (t), 59.3 (t), 111.6 (d), 166.9 (s), 168.9 (s). − MS (70 eV); *m*/*z*: 210 (32) [M$^+$] , 165 (31), 153 (100), 125 (84), 107 (32). − HMRS: calcd. for $C_{13}H_{22}O_2$: 210.1619; found 210.1628.

Ethyl (3-Methylcyclohexylidene)acetate (4c): Prepared according to Procedure A using cyclohexenone and phosphonate **3a** as substrates. Liquid (0.35 g, 85%); *E*/*Z* = 50:50. − IR: $\tilde{\nu}$ = 2935, 2860, 1720, 1655, 1455, 1380, 1215, 1155 cm^{-1}. − ^{1}H NMR ($CDCl_3$): Mixture of *E* + *Z* isomers: δ = 0.88 (d, 1.5 H, *J* = 6.5 Hz), 0.90 (d, 1.5 H, *J* = 6.2 Hz), 1.19 (t, 3 H, *J* = 7.2 Hz), 1.25−2.20 (m, 8 H), 3.50−3.62 (m, 1 H), 4.06 (q, 2 H, *J* = 7.2 Hz), 5.52 (s, 0.5 H), 5.54 (s, 0.5 H). − ^{13}C NMR ($CDCl_3$): *E* + *Z* isomers: δ = 14.2 (q), 22.0 (q), 22.1 (q), 26.4 (t), 27.2 (t), 29.1 (t), 34.5 (t), 34.0 (d), 34.7 (d), 37.4 (t), 37.7 (t), 46.0 (t), 59.3 (t), 113.2 (d), 162.6 (s), 166.7 (s). − MS (70 eV); *m*/*z* (%): 182 (100) [M$^+$], 167 (45), 154 (50), 149 (24), 139 (55), 137 (73), 121 (38), 109 (23), 103 (29). − HRMS: calcd. for $C_{11}H_{18}O_2$: 182.1307; found 182.1313.

Ethyl 2-(3-Methylcyclohexylidene)propionate (4d): Prepared according to Procedure A using cyclohexenone and phosphonate **3b** as substrates. Liquid (0.38 g, 85%); *E*/*Z* = 50:50. − IR (neat): $\tilde{\nu}$ = 2922, 2872, 1718, 1645, 1455, 1380, 1265, 1205, 1155 cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 0.91 (d, 1.5 H, *J* = 6.1 Hz), 0.94 (d, 1.5 H, *J* = 6.1 Hz), 1.28 (t, 1.5 H, *J* = 7.2 Hz), 1.29 (t, 1.5 H, *J* = 7.2 Hz), 1.41−1.85 (m, 7 H), 1.84 (s, 3 H), 2.48−2.60 (m, 1 H), 2.81−2.93 (m, 1 H), 4.17 (q, 2 H, *J* = 7.2 Hz). − ^{13}C NMR ($CDCl_3$): δ = 14.2 (q), 15.0 (q), 22.1 (q), 26.4 (t), 26.9 (t), 30.5 (t), 31.7 (t), 33.7 (d), 34.1 (d), 39.2 (t), 40.4 (t), 60.0 (t), 119.9 (s), 146.6 (s), 1706 (s). − MS (70 eV); *m*/*z* (%): 196 (100) [M$^+$], 168 (37), 167 (28), 151 (85), 150 (78), 149 (45), 135 (47), 131 (33), 121 (40), 111 (32),107 (30). − $C_{12}H_{20}O_2$ (196): calcd. C 73.43, H 10.27; found C 73.46, H 10.60.

Ethyl (3-Butylcyclohexylidene)acetate (4e):[19] Prepared according to Procedure A using cyclohexenone and phosphonate **3a** as substrates and *n*-butyllithium instead of methyllithium. Liquid (0.47 g, 93%); *E*/*Z* = 50:50. − IR (neat): $\tilde{\nu}$ = 2935, 2860, 1715, 1655, 1440, 1740, 1215, 1155 cm^{-1}. − ^{1}H NMR ($CDCl_3$): Mixture of *E* + *Z* isomers: δ = 0.89 (t, 3 H, *J* = 6.5 Hz), 1.26 (t, 1.5 H, *J* = 7.2 Hz), 1.27 (t, 1.5 H, *J* = 7.2 Hz), 1.02−1.55 (m, 9 H), 1.60−2.33 (m, 5 H), 3.62 (d, 0.5 H, *J* = 16.8 Hz), 3.70 (d, 0.5 H, *J* = 16.5 Hz), 4.13 (q, 1 H, *J* = 7.2 Hz), 4.14 (q, 1 H, *J* = 7.2 Hz), 5.60 (s, 1 H). −

^{13}C NMR ($CDCl_3$): Mixture of *E* and *Z* isomers: δ = 13.9 (q), 14.1 (q), 22.7 (t), 26.4 (t), 27.2 (t), 28.8 (t), 29.4 (t), 32.1 (t), 35.9 (t), 36.2 (t), 36.3 (t), 37.7 (t), 39.0 (d), 39.7 (d), 44.1 (t), 59.2 (t), 113.1 (d), 162.7 (s), 162.8 (s), 166.6 (s). − MS (70 eV); *m*/*z* (%): 224 (57) [M^+], 179 (35), 167 (100), 139 (48), 121 (33). − $C_{14}H_{24}O_2$ (224): calcd. C 74.95, H 10.78; found C 74.74, H 11.28.

Ethyl (3-Phenylcyclohexylidene)acetate (4f):[20] Prepared according to Procedure A using cyclohexenone and phosphonate **3a** as substrates and phenyllithium instead of methyllithium. Solid (0.53 g, 96%); *E*/*Z* = 50:50. − IR (neat): $\tilde{\nu}$ = 2920, 2850, 1718, 1643, 1441, 1380, 1155, 1040 cm^{-1}. − ^{1}H NMR ($CDCl_3$): Mixture of *E* + *Z* isomers: δ = 1.25 (t, 3 H, *J* = 7.1 Hz), 1.28 (t, 3 H, *J* = 7.0 Hz), 1.40−2.52 (m, 2 × 6 H), 2.60−2.79 (m, 2 × 1 H), 3.90 (d, 1 H, 16.0 Hz), 4.01 (dd, 1 H, *J* = 1.2 Hz and 16.0 Hz), 4.12 (q, 2 H, *J* = 7.0 Hz), 4.16 (q, 2 H, *J* = 7.1 Hz), 5.67 (s, 1 H), 5.69 (s, 1 H), 7.11−7.42 (m, 2 × 5 H). − ^{13}C NMR ($CDCl_3$): Mixture of *E* + *Z* isomers: δ = 14.3 (q), 27.1 (t), 27.8 (t), 29.1 (t), 33.7 (t), 33.9 (t), 36.9 (t), 37.3 (t), 45.2 (d), 46.2 (d), 59.5 (t), 59.6 (t), 113.8 (d) , 113.9 (d), 126.1 (d), 126.4 (d), 126.6 (d), 126.7 (d), 127.1 (d), 127.2 (d), 128.1 (d), 128.3 (d), 128.5 (d), 128.7 (d), 145.8 (s), 145.9 (s), 161.6 (s), 161.8 (s), 166.7 (s). − MS (70 eV); *m*/*z* (%): 244 (86) [M^+], 199 (36), 171 (56), 170 (37), 154 (32), 153 (34), 129 (29), 118 (46), 117 (100). − $C_{16}H_{20}O_2$ (244): calcd. C 78.65, H 8.25; found C 78.63, H 8.55.

Ethyl (3,3-Dimethylcyclopentylidene)acetate (4g): Prepared according to Procedure A using 3-methylcyclopentenone and phosphonate **3a** as substrates. Liquid (0.34 g, 82%); *E*/*Z* = 73:27. − IR (neat): $\tilde{\nu}$ = 2950, 2870, 1710, 1655, 1455, 1370, 1200, 1125 cm^{-1}. − ^{1}H NMR ($CDCl_3$): *E* isomer: δ = 0.97 (s, 6 H), 1.29 (t, 3 H, *J* = 6.8 Hz), 1.58 (t, 2 H, *J* = 7.6 Hz), 2.24 (s, 2 H), 2.84 (t, 2 H), 4.18 (q, 2 H, *J* = 6.8 Hz), 5.70 (m, 1 H). − *Z* isomer: δ = 1.00 (s, 6 H), 1.28 (t, 3 H, *J* = 7.2 Hz), 1.50 (t, 2 H, *J* = 7.6 Hz), 2.56 (t, 2 H), 2.62 (s, 2 H), 4.17 (q, 2 H, *J* = 7.2 Hz), 5.70 (m, 1 H). − ^{13}C NMR ($CDCl_3$): *E* isomer: δ = 14.3 (q), 27.2 (q), 31.3 (t), 38.1 (s), 38.8 (t) 47.4 (t), 59.3 (t) 112.2 (d) 166.9 (s) 169.1 (s). − *Z* isomer: δ = 14.3 (q), 27.9 (q), 33.8 (t), 39.2 (s), 39.8 (t), 50.5 (t) 59.4 (t) 112.5 (d), 166.8 (s), 168.8 (s). − MS (70 eV) *m*/*z* (%): 182 (65) [M^+], 167 (95), 151 (95), 150 (100), 139 (95), 135 (100), 121 (53), 112 (82), 109 (80). − HRMS: calcd. for $C_{11}H_{18}O_2$: 182.13068; found 182.13609.

Ethyl 2-(3,3-Dimethylcyclohexylidene)acetate (4h):[21] Prepared according to Procedure A using 3-methylcyclohexenone and phosphonate **3a** as substrates. Liquid (0.37 g, 83%); *E*/*Z* = 77:23. − IR (neat): $\tilde{\nu}$ = 2945, 1715, 1645, 1455, 1380, 1210, 1150 cm^{-1}. − ^{1}H NMR ($CDCl_3$): *E* isomer: δ = 0.91 (s, 3 H), 1.29 (t, 3 H, *J* = 6.8 Hz), 1.38−1.71 (m, 4 H), 1.97 (s, 2 H), 2.78 (dt, 2 H, *J* = 1.1 and 6.8 Hz), 4.15 (q, 2 H, *J* = 6.8 Hz), 5.57 (t, 1 H, 1.1 Hz). − *Z* isomer: δ = 0.94 (s, 3 H), 1.28 (t, 3 H, *J* = 7.2 Hz), 1.38−1.70 (m, 4 H), 2.14 (dt, 2 H, *J* = 1.1 Hz and 6.5 Hz), 2.64 (s, 2 H), 4.14 (q, 2 H, *J* = 7.2 Hz), 5.70 (t, 1 H, *J* = 1.1 Hz). − ^{13}C NMR ($CDCl_3$): *E* isomer: δ = 14.2 (q), 23.3 (q), 24.2 (q), 28.4 (t), 34.3 (s), 37.5 (t), 38.9 (t), 51.0 (t), 59.4 (t), 114.3 (d), 161.9 (s), 168.5 (s). − *Z* isomer: δ =14.2 (q), 23.2 (q), 24.2 (q), 29.1 (t), 34.3 (s), 39.2 (t), 42.3 (t), 59.3 (t), 114.4 (d), 161.9 (s), 168.5 (s). − MS (70 eV); *m*/*z* (%): 196 (100) [M^+], 181 (63), 167 (100), 153 (46), 151 (71), 139 (55), 128 (50), 121 (55), 107 (57). − HRMS: calcd. for $C_{12}H_{20}O_2$: 196.1463; found 196.1458.

Ethyl (3,3,5,5-Tetramethylcyclohexylidene)acetate (4i): Prepared according to Procedure A using isophorone and phosphonate **3a** as substrates. Liquid (0.42 g, 83%). − IR (neat): $\tilde{\nu}$ = 2592, 1716, 1647, 1459, 1376, 1230, 1155, 1040 cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 0.96 (s, 6 H), 0.98 (s, 6 H), 1.28 (t, 3 H, *J* = 7.2 Hz), 1.34 (s, 2 H), 1.98 (s, 2 H), 2.62 (s, 2 H), 4.15 (q, 2 H, *J* = 7.2 Hz), 5.69 (t, 1 H, *J* = 0.8 Hz). − ^{13}C NMR ($CDCl_3$): δ = 14.2 (q), 30.7 (q), 30.8 (q), 34.7 (s), 34.9 (s), 42.2 (t), 51.1 (t), 52.5 (t), 59.4 (t), 115.8 (d), 160.3 (s), 166.5 (s). − MS (70 eV); *m*/*z* (%): 224 (46) [M^+], 209 (100), 181 (22), 179 (24), 163 (27), 125 (22), 111 (29). − $C_{14}H_{24}O_2$ (224): calcd. C 74.95, H 10.78; found C 75.12, H 11.18.

(*E*)-Ethyl 5-Phenyl-2-hexenoate (5a):[22] Prepared from *trans*-cinnamaldehyde according to Procedure B. Liquid (0.23 g, 47%). − ^{1}H NMR ($CDCl_3$): δ = 1.29 (t, 3 H, *J* = 7.1 Hz), 1.31 (d, 3 H, *J* = 6.5 Hz), 2.31−2.62 (m, 2 H), 2.88 (sext, 1 H, *J* = 6.5 Hz), 4.16 (q, 2 H, *J* = 7.1 Hz), 5.78 (dt, 1 H, *J* = 15.7 Hz and 1.4 Hz), 6.88 (dt, 1 H, *J* = 15.7 Hz and 6.7 Hz), 7.11−7.35 (m, 5 H). − ^{13}C NMR ($CDCl_3$): δ = 14.1 (q), 21.5 (q), 39.1 (d), 40.8 (t), 60.0 (t), 122.6 (d), 126.2 (d), 126.7 (d), 128.4 (d), 146.0 (s), 147.1 (d), 166.4 (s).

Ethyl 3-Methyl-5-phenyl-2-hexenoate (5b): Prepared from 4-phenyl-3-buten-2-one according to Procedure B. Liquid (0.38 g, 72%); *E*/*Z* = 87:13. − IR (neat): $\tilde{\nu}$ = 2966, 2931, 2872, 1713, 1602, 1493, 1450, 1376, 1350, 1223 cm^{-1}. − ^{1}H NMR ($CDCl_3$): *E* isomer: δ = 1.26 (t, 3 H, *J* = 7.2 Hz), 2.13 (d, 3 H, *J* = 1.1 Hz), 2.32 (ddd, 1 H, J_{AB} = 13.3 Hz, *J* = 8.4 Hz and 1.1 Hz), 2.46 (ddd, 1 H, J_{AB} = 13.3 Hz, *J* = 6.5 Hz and 1.0 Hz), 3.02 (sext, 1 H, *J* = 6.9 Hz), 4.12 (q, 2 H, *J* = 7.2 Hz), 5.61 (q, 1 H, *J* = 1.1 Hz), 7.14−7.34 (m, 5 H). − *Z* isomer: δ = 1.24 (t, 3 H, *J* = 7.2 Hz), 1.70 (d, 3 H, *J* = 1.1 Hz), 2.74 (dd, 1 H, J_{AB} = 11.8 Hz, *J* = 7.2 Hz), 3.02 (sext, 1 H, *J* = 6.9 Hz), 3.14 (ddd, 1 H, J_{AB} = 12.2 Hz, *J* = 8.4 Hz, *J* = 1.1 Hz), 4.13 (q, 2 H, *J* = 7.2 Hz), 5.65 (s, 1 H), 7.14−7.34 (m, 5 H). − ^{13}C NMR ($CDCl_3$): *E* isomer: δ = 14.3 (q), 18.6 (q), 21.4 (q), 37.8 (d), 49.9 (t), 59.4 (t), 117.4 (d), 126.2 (d), 126.8 (d), 128.5 (d), 146.4 (s), 157.9 (s), 166.6 (s). − MS (70 eV); *m*/*z* (%): 232 (60) [M^+], 187 (61), 158 (100), 145 (42), 129 (65), 104 (94), 102 (93). − HRMS: calcd. for $C_{15}H_{20}O_2$: 232.1463; found 232.1467.

(*E*)-Ethyl 3-(2-Methylcyclohexyl)propenoate (5c): Prepared from 1-cyclohexenecarboxaldehyde according to Procedure A. Liquid (0.29 g, 65%); *Z*/*E* = 32:68. − ^{1}H NMR ($CDCl_3$): *Z* isomer: δ = 0.84 (d, 3 H, *J* = 7.0 Hz), 1.30 (t, 3 H, *J* = 7.2 Hz), 1.10−1.90 (m, 9 H), 2.30−2.45 (m, 1 H), 4.18 (q, 2 H, *J* = 7.2 Hz), 5.78 (dd, 1 H, *J* = 0.6 and 15.6 Hz), 6.81 (dd, 1 H, *J* = 9.1 and 15.6 Hz). − *E* isomer: δ = 0.85 (d, 3 H, *J* = 7.0 Hz), 1.30 (t, 3 H, *J* = 7.2 Hz), 1.10−1.90 (m, 9 H), 4.19 (q, 2 H, *J* = 7.2 Hz), 5.79 (dd, 1 H, *J* = 0.6 Hz and 15.6 Hz), 7.8 (dd, 1 H, *J* = 8.0 and 15.7 Hz). − ^{13}C NMR ($CDCl_3$): *E* isomer: δ = 14.2 (q), 20.8 (q), 23.3 (t), 25.6 (t), 33.7 (d), 34.3 (d), 43.2 (t), 60.0 (t), 121.0 (d), 151.6 (d), 166.8 (s). − *Z* isomer: δ = 14.2 (q), 16.8 (q), 23.3 (t), 26.1 (t), 28.3 (t), 32.3 (d), 36.3 (d), 48.5 (t), 60.0 (t), 120.5 (d), 153.6 (d), 168.8 (s). − $C_{12}H_{20}O_2$ (196): calcd. C 73.42, H 10.27; found C 73.41, H 10.67.

(*E,E*)-Ethyl 5,5,9-Trimethyl-2,8-decanedienoate (5d):[23] Prepared from geranial according to Procedure A. Liquid (0.44 g, 81%); *E*/*Z* = 100:0. − IR (neat): $\tilde{\nu}$ = 2960, 2925, 1720, 1650, 1465, 1365, 1205, 1190, 1150, 1050 cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 0.92 (s, 6 H), 1.15−1.30 (m, 2 H), 1.29 (t, 3 H, *J* = 7.1 Hz), 1.60 (s, 3 H), 1.68 (s, 3 H), 1.93 (dt, 2 H, *J* = 8.96 and 7.5 Hz), 2.10 (dd, 2 H, *J* = 7.9 and 1.3 Hz), 4.18 (q, 2 H, *J* = 7.1 Hz), 5.08 (tt, 1 H, *J* = 1.3 and 7.1 Hz), 5.81 (dt, 1 H, 15.5 and 1.3 Hz), 6.98 (dt, 1 H, *J* = 15.5 and 7.9 Hz). − ^{13}C NMR ($CDCl_3$): δ = 14.25 (q), 17.5 (q), 22.7 (t), 25.6 (q), 26.9 (q), 33.8 (s), 42.03 (t), 44.7 (t), 60.08 (t), 123.3 (d), 124.7 (d), 131.1 (s), 146.5 (d), 166.4 (s). − MS (70 eV) *m*/*z* (%): 238 (31) [M^+], 223 (33), 195 (28), 164 (33), 155 (69), 150 (61), 142 (56), 123 (84), 114 (95), 109 (100). − $C_{15}H_{26}O_2$ (238): calcd. C 75.58, H 10.99; found C 75.26, H 11.21.

(*E,E*)-Ethyl 5,9-Dimethyl-2,8-decanedienoate (5e):[24] A solution of methyllithium (1.6 M, 0.15 mL, 0.225 mmol) was added at −65 °C to a suspension of CuI (43 mg, 0.225 mmol) in THF (12.5 mL). To the obtained yellow solution of MeCu was first added HMPA (2.5 mL) followed by an *n*-hexane solution of DIBAL (1 M, 2.5 mL, 2.5 mmol). After being stirred for 30 min at the same temperature, geranial (0.34 g, 2.25 mmol) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 3 h and allowed to warm up to −20 °C. Diethyl ethoxycarbonyl(methyl)phosphonate (**3a**) (0.50 g, 2.25 mmol) was then introduced in one portion and the resulting mixture was stirred overnight at room temp. After treatment with a 1 N HCl solution and diethyl ether (50 mL), the two layers were separated and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The separated ethereal solution was then washed with brine (15 mL), dried with anhydrous magnesium sulfate, filtered and concentrated under vacuum. The crude product was purified by flash chromatography on silica (eluent: AcOEt/hexanes, 7:93), giving **5e** (0.20 g, 41%) as a liquid; *E*/*Z* = 50:50 − IR (neat): $\tilde{\nu}$ = 2960, 2873, 1722, 1653, 1455, 1375, 1305, 1285, 1045cm^{-1}. − ^{1}H NMR ($CDCl_3$): *E* + *Z* isomers: δ = 0.91 (d, 3 H, *J* = 6.1 Hz), 1.28 (t, 3 H, *J* = 7.2 Hz), 1.62 (s, 3 H), 1.69 (s, 3 H), 1.60−2.55 (m, 7 H), 4.18 (q, 2 H, *J* = 7.2 Hz), 5.08 (tq, 1 H, *J* = 7.1 Hz and 1.4 Hz), 5.78 (dd, 0.5 H, *J* 1.5 and 15.6 Hz), 5.81 (dt, 0.5 H, *J* = 15.6 Hz and 1.5 Hz), 6.94 (dt, 0.5 H, *J* = 15.6 Hz and 7.5 Hz), 6.96 (dd, 0.5 H, *J* = 15.6 Hz and 6.5 Hz). − MS (70 eV); *m*/*z* (%): 224 (23) [M$^+$], 181 (24), 156 (57), 142 (100), 136 (65), 126 (45), 114 (43), 109 (90).

(*E*)-Ethyl 3-(Cyclohex-1-enyl)propenoate (6):[25] To a suspension of NaH (0.26 g, 11 mmol) in diethyl ether (150 mL) was added at room temp. diethyl ethoxycarbonylphosphonate (2.47 g, 11 mmol). After complete deprotonation (no hydrogen gas evolution), 1-cyclohexenylcarboxaldehyde[26] (1.10 g, 10 mmol), diluted in the same solvent (10 mL), was added dropwise. The mixture was stirred for 2.5 h and hydrolyzed with a 1 N HCl solution. After separation of the two phases and extraction of the aqueous layer with diethyl ether, the ethereal layers were combined, dried with $MgSO_4$, filtered and concentrated. The residue was purified by flash-chromatography on silica (eluent: AcOEt/hexanes, 7:93), giving pure **6** as a liquid (1.54 g, 78%). − IR (neat): $\tilde{\nu}$ = 2980, 2931, 2860, 1713, 1628, 1447, 1368, 1307, 1265, 1245, 1166, 1040, 982 cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 1.29 (t, 3 H, *J* = 7.2 Hz), 1.50−1.76 (m, 4 H), 2.05−2.22 (m, 4 H), 4.20 (q, 2 H, *J* = 7.2 Hz), 5.76 (d, 1 H, *J* = 15.7 Hz), 6.16 (s, 1 H), 7.28 (d, 1 H, *J* = 15.7 Hz). − ^{13}C NMR ($CDCl_3$): δ = 14.2 (q), 21.9 (t), 24.0 (t), 26.3 (t), 59.9 (t), 114.5 (d), 134.8 (s), 138.5(d), 147.9 (d), 167.5 (s). − MS (70 eV); *m*/*z* (%): 196 (4) [M$^+$], 194 (8), 180 (100), 167 (25), 152 (52), 151 (80), 142 (26), 135 (77), 123 (27), 121 (42), 107 (76), 105 (64).

Ethyl [3-(2,6-Dithiacyclohexyl)cyclohexylidene]acetate (7a): To a solution of 1,3-dithiane (0.45 g, 3.79 mmol) in THF (4 mL) under argon was added at −80 °C a solution of *n*-butyllithium in hexane (1.6 M, 2.37 mL, 3.79 mmol). The reaction mixture was stirred and the temperature allowed to rise to −20 °C. After cooling to −80 °C, HMPA (1.32 mL, 7.58 mmol) was then added, followed by cyclohexenone (0.37 mL, 3.79 mmol) in THF (5 mL). After 3 h at this temperature, phosphonate **3a** was introduced and the mixture was stirred overnight at room temp. Acidic hydrolysis was performed using a 1 N HCl solution. After separation of the two phases, the aqueous layer was extracted twice with diethyl ether (40 mL). The combined ether solutions were dried with $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica employing AcOEt/hexanes (10:90) as eluent to give **7a** (0.85 g, 78%); *E*/*Z* = 55:45. − IR ($CHCl_3$): $\tilde{\nu}$ = 2958, 2897, 1716, 1647, 1457, 1376, 1229, 1154, 1043. − ^{1}H NMR ($CDCl_3$): Mixture of *E* + *Z* isomers: δ = 1.27 (t, 3 H, *J* = 7.1 Hz), 1.28−1.65 (m, 2 H), 1.78−2.20 (m, 7 H), 2.24 (d, 0.55 H, *J* = 12.8 Hz), 2.45 (d, 0.45 H, *J* = 12.9 Hz), 2.86 (m, 4 H), 3.67 (d, 0.55 H, *J* = 12.6 Hz), 3.98 (d, 0.45 H, *J* = 12.2 Hz), 4.06−4.22 (m, 3 H), 5.64 (s, 1 H). − ^{13}C NMR ($CDCl_3$): Mixture of *E* + *Z* isomers: δ = 14.3 (q), 26.2, 26.3 (t), 27.1 (t), 29.2 (t), 29.4 (t), 29.7 (t), 30.7, 30.9 (t), 33.6 (t), 37.2 (t), 41.0 (t), 44.1 (d), 44.4 (d), 53.8 (d), 54.4 (d), 59.6 (t), 114.3, 114.5 (d), 160.8, 160.9 (s), 166.53 (s). − MS (70 eV), *m*/*z* (%): 286 (34) [M$^+$], 241 (16), 180 (13), 167 (47),121 (23), 120 (34), 119 (100). − $C_{14}H_{22}O_2S_2$ (286): calcd. C 58.70, H 7.74; found C 58.25, H 7.85.

Ethyl [3-(Dimethylmalonyl)cyclohexylidene]acetate (7b): Dimethyl malonate (0.38 mL, 3.30 mmol) was added dropwise at 0 °C to a suspension of NaH (0.13 g, 3.3 mmol) in diethyl ether (30 mL). After 1 h and complete deprotonation, HMPA (1.04 mL, 6 mmol) was added in one portion; and after cooling to −50 °C, cyclohexenone (0.29 mL, 3 mmol) was slowly added. The reaction mixture was stirred for an additional 3 h. Phosphonate **3a** (1.34 g, 6.0 mmol) was introduced and the resulting mixture was stirred overnight at room temp. After hydrolysis with a 1 N HCl solution and addition of diethyl ether (50 mL), the aqueous layer was extracted with the same solvent. The combined organic layers were dried with $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica employing AcOEt/hexanes (10:90) as eluent to give **7b** (0.83 g, 92%) as a solid, m.p. 63−65 °C; *E*/*Z* = 60:40. − IR ($CHCl_3$): $\tilde{\nu}$ = 2985, 1740, 1713, 1645, 1445, 1375, 1360, 1265, 1245, 1220, 1175 cm^{-1}. − ^{1}H NMR ($CDCl_3$): *E* isomer: δ = 1.27 (t, 3 H, *J* = 7.1 Hz), 1.10−1.60 (m, 2 H), 1.70−2.50 (m, 6 H), 3.30 (d, 1 H, *J* = 8.3 Hz), 3.63 (d, 1 H, *J* = 14 Hz), 3.74 (s, 3 H), 3.75 (s, 3 H), 4.14 (q, 2 H, *J* = 7.1 Hz), 5.63 (sl, 1 H). − *Z* isomer: δ = 1.26 (t, 3 H, *J* = 7.0 Hz), 1.10−1.60 (m, 2 H), 1.70−2.50 (m, 6 H), 3.39 (d, 1 H, *J* = 8.7 Hz), 3.64 (d, 1 H, *J* = 13 Hz), 3.76 (s, 3 H), 3.77 (s, 3 H), 4.13 (q, 2 H, *J* = 7.0 Hz), 5.66 (s, 1 H). − ^{13}C NMR ($CDCl_3$): Mixture of *E* and *Z* isomers: δ = 14.3 (q), 25.8, 26.5 (t), 29.0 (t), 29.6, 29.9 (t), 33.0, 37.1 (t), 38.5, 39.1 (d), 52.4 (q), 56.7, 56.8 (d), 59.5 (t), 114.8 (d), 159.6, 159.9 (s), 166.3, 166.4 (s), 168.6 (s). − MS; *m*/*z* (%): 299 (28) [M$^{+\cdot}$ + 1], 298 (15), 267 (13), 253 (54), 252 (77), 221 (55), 192 (56), 168 (49), 167 (100), 166 (57), 139 (74), 138 (47), 133 (71), 132 (75), 121 (100). − $C_{15}H_{22}O_6$ (298): calcd. C 60.39, H 7.43; found C 60.06, H 7.45.

Ethyl 2-Fluoro-2-(3,3,5,5-tetramethylcyclohexylidene)acetate (7c): Prepared according to Procedure A using isophorone and fluorophosphonate **3c** as substrates. Liquid (0.35 g, 64%). − IR (neat): $\tilde{\nu}$ = 2955, 2898, 2844, 1725, 1662, 1478, 1462, 1380, 1368, 1302, 1274, 1232, 1191, 1150, 1106, 1041. − ^{1}H NMR ($CDCl_3$): δ = 0.98 (s, 12 H), 1.31 (s, 2 H), 1.34 (t, 3 H, *J* = 7.1 Hz), 2.12 (d, 2 H, J_{H-F} = 2.7 Hz), 2.52 (d, 2 H, J_{H-F} = 1.3 Hz), 4.28 (q, 2 H, *J* = 7.1 Hz). − ^{13}C NMR ($CDCl_3$): δ = 14.1 (q), 30.7 (q), 30.8 (q), 34.6 (s), 34.7 (s), 40.7 (t), 41.0 (td, J_{C-F} = 8 Hz), 52.5 (t), 60.9 (t), 133.8 (s), 142.87 (d, J_{C-F} = 347 Hz), 161.53 (d, J_{C-F} = 44.5 Hz). − ^{19}F NMR: δ = −129.5 (s). − MS (70 eV); *m*/*z* (%): 242 (65) [M$^+$], 227 (100), 199 (51), 153 (27), 149 (87), 143 (33).

***N*-Methoxy-*N*-methyl-2-(3-methylcyclohexylidene)acetamide (7d):** Prepared according to Procedure A using cyclohexenone and phosphonate **3d** as substrates. Purification performed on silica employing AcOEt/hexanes (15:85) as eluent. Liquid (0.36 g, 82%); *E*/*Z* = 52:48. − IR (neat): $\tilde{\nu}$ = 2930, 2870, 1655, 1638, 1447, 1385, 1330, 1180, 1105 cm^{-1}. − ^{1}H NMR ($CDCl_3$): Mixture of *E* + *Z* isomers: δ = 0.94 (d, 1.5 $H_{(E)}$, *J* = 3.5 Hz), 0.97 (d, 1.5 $H_{(Z)}$, *J* = 3.2 Hz), 1.01−2.10 (m, 6 H), 2.12 (dd, 0.5 $H_{(Z)}$, *J* = 4.5 Hz and

12.2 Hz), 2.27 (dd, 0.5 $H_{(E)}$, J = 12.8 Hz), 3.20 (s, 3 H), 3.51 (t, 2 H, J = 9.7 Hz), 3.68 (s, 3 H), 6.02 (s, 1 H). − ^{13}C NMR ($CDCl_3$): E + Z isomers: δ = 22.1, 22.2, 26.6, 27.4, 29.4, 32.2, 34.6, 34.7, 34.8, 37.6, 38.0, 46.3, 61.2, 111.8, 111.9 (d), 159.0 (s), 167.1 (s). − MS (70 eV); *m/z* (%): 198 (65) [$M^{+\cdot}$ + 1], 197 (37), 141 (21), 137 (100), 136 (47). − $C_{11}H_{19}NO_2$ (197): calcd. C 66.97, H 9.70, N 7.10; found C 67.45, H 8.64, N 7.14.

2-(3-Methylcyclohexylidene)butyrolactone (7e): Prepared according to Procedure A using cyclohexenone and phosphonate **3e** as substrates. Viscous liquid (0.39 g, 97%). − IR ($CHCl_3$): ṽ = 2945, 1730, 1655, 1445, 1375, 1345, 1280, 1255, 1208, 1185, 1090, 1060, 1030 cm^{-1}. − ^{1}H NMR ($CDCl_3$): E + Z isomers: δ = 0.90 (d, 3 H, J = 6.9 Hz), 1.05−2.00 (m, 5 H), 2.34 (dd, 2 H, J = 13.2 Hz and J = 1.5 Hz), 2.87 (tq, 2 H, J = 8.1 Hz and J = 1.4 Hz), 3.85 (d, 1 H, J = 15.5 Hz), 3.91 (d, 1 H, J = 12.5 Hz), 4.25 (t, 2 H, J = 7.4 Hz). − ^{13}C NMR ($CDCl_3$): Mixture of E + Z isomers: δ = 22.0, 22.1 (q), 26.4, 26.6 (t), 27.1 (t), 27.8 (t), 33.7, 34.09 (d), 34.2, 34.3 (t), 36.2, 42.3 (t), 64.2 (t), 115.3 (s), 156.9 (s), 170.6 (s). − MS (70 eV); *m/z* (%): 180 (100) [$M^{+\cdot}$], 179 (22), 165 (100), 164 (22), 137 (27), 119 (16), 112 (14). − $C_{11}H_{16}O_2$ (180): C 73.30, H 8.94; found C 73.47, H 8.47.

***N*-Methoxy-*N*-methyl-2-(3,3-dimethylcyclohexylidene)acetamides (8a/8b):** Compounds **8a** and **8b** were prepared according to Procedure A using 3-methylcyclohexenone (0.60 g, 5.5 mmol) and phosphonate **3e** (2.68 g, 10.99 mmol) as substrates. Purification was achieved by flash chromatography on silica using AcOEt/hexanes (15:85) as eluent to give **8a/8b** as a liquid (1.04 g, 89%); Z/E = 40:60. − IR ($CHCl_3$): ṽ = 3415, 2936, 2873, 2860, 1655, 1454, 1386, 1346, 1315, 1178, 1100, 960 cm^{-1}. − ^{1}H NMR ($CDCl_3$): E isomer: δ = 0.90 (s, 6 H), 1.39 (t, 2 H, J = 6.5 Hz), 1.60 (quint, 2 H, J = 6.4 Hz), 1.98 (s, 2 H), 2.70 (t, 2 H, J = 6.2 Hz), 3.21 (s, 3 H), 3.67 (s, 3 H), 5.99 (s, 1 H). Z isomer: δ = 0.92 (s, 6 H), 1.40 (t, 2 H, J = 6.5 Hz), 1.65 (quint, 2 H, J = 6.2 Hz), 2.15 (t, 2 H, J = 6.5 Hz), 2.57 (s, 2 H), 2.69 (t, 2 H, J = 6.1 Hz), 3.19 (s, 3 H), 3.68 (s, 3 H), 6.11 (s, 1 H). − ^{13}C NMR ($CDCl_3$): E isomer: δ = 23.3 (t), 28.4 (2 q), 29.4 (t), 32.2 (s), 34.1 (t), 39.1 (t), 51.3 (t), 61.3 (q), 113.1 (d), 158.0 (s), 167.9 (s). − Z isomer: δ = 24.2 (t), 28.3 (2 q), 31.8 (s), 34.0 (t), 37.7 (t), 39.3 (t), 42.5 (q), 61.3 (q), 113.2 (d), 158.2 (s), 167.9 (s). − MS (70 eV); *m/z* (%): 211 (3) [$M^{+\cdot}$], 196 (11), 181 (10), 168 (23), 151 (76), 137 (74), 109 (100).

2-Ochtoden-1-als (9a/9b):[14] A solution of DIBAL in toluene (1.2 M, 8.7 mL, 10.4 mmol) was added at −70 °C to a 15:85 solution of amides **8a** and **8b** (1.10 g, 5.2 mmol), dissolved in THF (50 mL). After being stirred for 1 h, an aqueous saturated ammonium chloride solution (20 mL) was added. The reaction mixture was slowly warmed up to 0 °C. After 2 h, the reaction mixture was acidified using a 1 N HCl solution. The aqueous solution was extracted with diethyl ether (4 × 50 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica, employing AcOEt/hexane (5:95) as eluent. Liquid (0.72 g, 91%). − IR ($CHCl_3$): ṽ = 2947, 2872, 1666, 1630, 1454, 1165, 1115 cm^{-1}. − ^{1}H NMR ($CDCl_3$): **9b**, E isomer: δ = 0.90 (s, 6 H), 1.43 (t, 2 H, J = 6.4 Hz), 1.69 (quint, 2 H, J = 6.2 Hz), 2.04 (s, 2 H), 2.61 (t, 2 H, J = 6.3 Hz), 5.76 (d, 1 H, J = 8.3 Hz), 9.99 (d, 1 H, J = 8.3 Hz). − **9a**, Z isomer: δ = 0.93 (s, 6 H), 1.43 (t, 2 H, J = 6.4 Hz), 1.69 (quint, 2 H, J = 6.2 Hz), 2.22 (t, 2 H, J = 6.4 Hz), 2.45 (s, 2 H), 5.90 (d, 1 H, J = 8.3 Hz), 9.94 (d, 1 H, J = 8.3 Hz). − ^{13}C NMR ($CDCl_3$): − **9b**, E isomer: δ = 23.7 (t), 28.4 (2q), 28.9 (t), 34.7 (s), 38.8 (t), 51.0 (t), 126.7 (d), 166.4 (s), 190.2 (s).

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