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An efficient synthesis of (*E*)-α,β-unsaturated ketones and esters with total stereoselectivity by using chromium dichloride

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Abstract—(*E*)-α,β-Unsaturated ketones **1** or esters **2** can be obtained with complete stereoselectivity by reaction of different 2-chloro-3-hydroxy ketones **3** or esters **4** and $CrCl_2$. A comparative study of the results of synthesis of ketones **1** with $CrCl_2$ or samarium is performed. A mechanism to explain both β-elimination reactions has been proposed.

1. Introduction

The development of methodologies for the formation of carbon–carbon double bonds could be considered one of the most important challenges in organic synthesis.[1]

α,β-Unsaturated ketones are one of the most useful starting materials to prepare different polifunctionalized organic compounds and have been widely used in organic synthesis.[2] The stereoselective synthesis of α,β-unsaturated ketones[3] has been extensively developed and is generally achieved by condensation,[4] oxidation,[5] elimination,[6] acylation[7] reactions, and by insertion of carbon monoxide[8] among others. However, in most of these syntheses, the stereoselective control of the carbon–carbon double bond formation remains unsolved. The poor yields or the difficult preparation of the starting materials also limit other methodologies.

Respect to α,β-unsaturated esters, its preparation[9] is generally achieved by C=C bond formation by Wittig,[10] Horner–Emmons,[11] Heck[12] or Peterson[13] reactions. Another useful approach employs the Cope rearrangement,[14] utilising acetylenic compounds[15] or using α-mercaptoesters derivatives.[16] However, most of these methodologies, give a mixture of diastereoisomers, and poor yields are obtained. In other cases, poor generality is a major limitation. In addition, the preparations of α,β-unsaturated esters in which C=C bond is trisubstituted are scarce.[17]

The sum of all theses features would make a general and highly stereoselective method to prepare α,β-unsaturated ketones and esters from easily available starting material of great interest.

Recently, we describe the preliminary results of a new methodology to obtain α,β-unsaturated esters **2** with total diastereoselectivity by treatment of the easily available α-halo-β-hydroxyesters **4** with chromium dichloride.[18] A $CrCl_2$-promoted sequential condensation–elimination reaction of various aldehydes with ethyl dibromoacetate to afford α,β-unsaturated esters in high yield and with total selectivity has been also published.[19] In addition, we have also reported a synthesis of α,β-unsaturated ketones from 2-chloro-3-hydroxy ketones by using SmI_2 or SmI_3.[20]

In the present work, as part of our interest on developing new selective syntheses of functionalized alkenes, we wish to extend these previous results and to explore the possible use of chromium dichloride to carry out other β-elimination reactions. Concretely, here we report the preparation of (*E*)-α,β-unsaturated ketones **1** and esters **2** with total stereoselectivity promoted by $CrCl_2$.

2. Results and discussion

2.1. Synthesis of α,β-unsaturated ketones 1

The treatment of a solution of 2-chloro-3-hydroxy ketones **3** in refluxing THF with 3 equiv of $CrCl_2$ during 4 h afforded, after acid hydrolysis,[21] the corresponding α,β-unsaturated ketones **1** in high yields and with total (*E*)-selectivity (Scheme 1 and Table 1).

Keywords: Diastereoisomers; α-β-unsaturated ketones; Ketones; Stereoselectivity; α,β-unsaturated esters.
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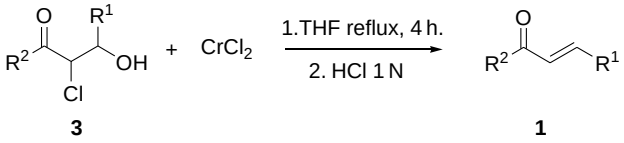


3 1

Scheme 1. Synthesis of (*E*)-α,β-unsaturated ketones **1**.

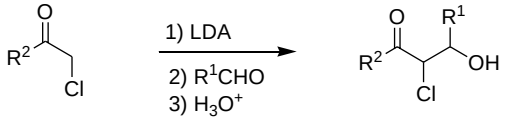
Table 1. Synthesis of (*E*)-α,β-unsaturated ketones **1**

Entry	1[a]	R^1	R^2	Yield		
				1 (%)[b]		**3** (%)[c]
				$CrCl_2$	SmI_2[d]	
1	**1a**	*n*-C_4H_9	Ph	81	96 (72)	82
2	**1b**	*n*-C_7H_{15}	Ph	84	98 (91)	85
3	**1c**	Cyclohexyl	Ph	91	67 (72)	93
4	**1d**	Ph	Ph	72	73 (80)	80
5	**1e**	*i*-Bu	Ph	85	—[e]	88
6	**1f**	$CH_3CH(Ph)$	Ph	68	—[e]	67
7	**1g**	*n*-C_4H_9	*n*-C_4H_9	77	—[e]	64
8	**1h**	Ph	*n*-C_4H_9	71	82 (70)	92
9	**1i**	*n*-C_4H_9	*t*-Bu	89	65 (58)	79
10	**1j**	4-MeO-Ph	Me	91	—[e]	61

[a] Three equivalents of $CrCl_2$ were used in all cases.
[b] Isolated yield based on the starting α-chloro-β-hydroxy ketones **3**.
[c] Isolated yield based on the starting α-chloroketones **5**.
[d] Isolated yield by using SmI_3, in parenthesis.
[e] This reaction was not performed by using SmI_2 or SmI_3.

The diastereoisomeric excess was determined on the crude products by ^{1}H NMR spectroscopy (300 MHz) and GC–MS, showing the presence of a single stereoisomer. The (*E*)-configuration of the C–C double bond in products **1** was assigned on the basis of ^{1}H NMR coupling constants observed for the olefinic protons.[22] These values are in agreement with those previously reported (**1a–d**).[20]

The starting ketones **3** were easily prepared by reaction of the corresponding lithium enolates of α-haloketones **5** with aldehydes at −78 °C[20] (Scheme 2 and Table 1).



5 3

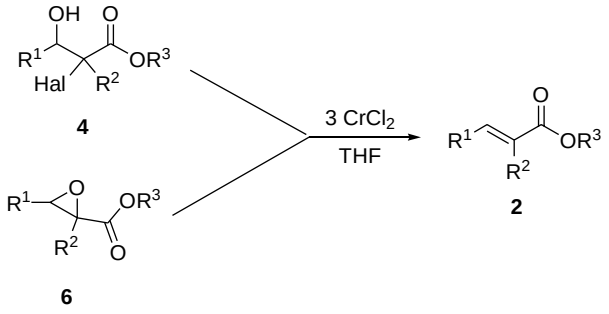
Scheme 2. Preparation of starting compounds **3**.

Several comments are worth of mention: (1) interestingly, although different mixtures of stereoisomers (ranging from 1:1 to 4:1) of starting materials **3** were used, the corresponding α,β-unsaturated ketones **1** were obtained with total (*E*)-stereoselectivity. (2) The method presents wide applicability. Both aromatic and aliphatic (linear, branched or cyclic) (*E*)-α,β-unsaturated ketones **1** can be obtained (Table 1). (3) In some cases (**1a–d**, **1i**) the crude reaction products were obtained with high purity and no purification by column chromatography was necessary.

As was previously described,[20] the same transformation (synthesis of (*E*)-α,β-unsaturated ketones **1** from the same α-chloro-β-hydroxy ketones **3**) can also accomplish by using SmI_3 or SmI_2. Results in Table 1 show that, in general, similar or slightly higher yields of α,β-unsturated ketones were obtained by using $CrCl_2$ instead of SmI_3 or SmI_2, the stereoselectivity being complete in both cases, the two proposed methods can be complementary and represent valuable methods for the preparation α,β-unsaturated ketones.

2.2. Synthesis of α,β-unsaturated esters 2

Our first attempts were carried out using α-chloro-β-hydroxyesters and α,β-epoxyesters in order to determine suitable starting materials. Thus, treatment of a solution of ethyl 2-chloro-3-hydroxy-2-methyldecanoate **4d** in THF with $CrCl_2$ at reflux during 4 h afforded ethyl 2-methyldecan-2-enoate **2d**, after hydrolysis, with total diastereoselectivity (de>98%) and 64% yield. The same treatment of 2,3-epoxy-2-methyl decanoate **6d**, gave **2d** with slightly lower diastereoselection (de 95%) and yield (51%). Based on these results, preparation of α,β-unsaturated esters was performed from compounds **4**. So, the treatment of different 2-halo-3-hydroxyesters **4** with $CrCl_2$ (3 equiv) at room temperature afforded (*E*)-α,β-unsaturated esters with total diastereoselectivity (Scheme 3). Table 2 summarizes the obtained results.



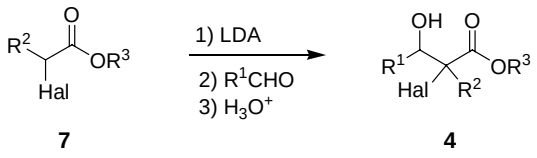
Scheme 3. Synthesis of (*E*)-α,β-unsaturated esters **2**.

Table 2. Synthesis of (*E*)-α,β-unsaturated esters **2**

Entry	2[a]	R^1	R^2	R^3	Hal	Yield	
						4 (%)[b]	**2** (%)[c]
1	**2a**	*n*-C_7H_{15}	H	Me	Cl	87	65
2	**2b**	*p*Cl–C_6H_4	H	Me	Cl	69	68
3	**2c**	MeCH(Ph)	H	Me	Cl	75	52
4	**2d**	*n*-C_7H_{15}	Me	Et	Cl	93	64
5	**2e**	Cyclohexyl	Me	Et	Cl	95	65
6	**2f**	Ph	Me	Et	Cl	97	60
7	**2g**	*p*MeO–C_6H_4	Me	Et	Cl	91	70
8	**2h**	Ph	*n*-C_6H_{13}	Et	Br	92	65
9	**2i**	Ph	*n*-C_5H_{11}	Et	Br	89	90
10	**2j**	Cyclohexyl	Me	*i*-Pr	Cl	84	70

[a] In all cases de was >98%. It was determinated on crude reaction products by ^{1}H NMR spectroscopy and GC–MS.
[b] Isolated yield after column chromatography based on compound **7**.
[c] Isolated yield after column chromatography based on compound **4**.

The starting materials **4** were easily prepared by reaction of the corresponding lithium enolates of α-haloesters **7** (generated by treatment of α-haloesters with LDA at −78 °C) with aldehydes at −78 °C (Scheme 4).



Scheme 4. Preparation of starting compounds **4**.

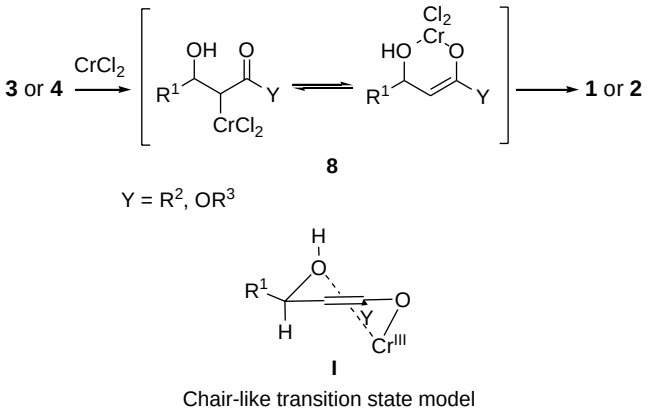
α,β-Unsaturated esters **2** were also obtained with total diastereoselectivity from mixtures of diastereoisomers (roughly 1:1) of the starting compounds **4**. ^{1}H NMR spectroscopy (300 MHz) and GC–MS of the crude reaction of products **2**, shown the presence of a single diastereoisomer.

The *E* stereochemistry in the C–C double bond of α,β-unsaturated esters **2** was assigned on the basis of the value of ^{1}H NMR coupling constants between the olefinic protons of compound **2a–c** (Table 2, entries 1–3);[23] by NOE experiments in the case of the trisubstituted compounds **2g**, and **2i** or by comparison with the ^{1}H and ^{13}C NMR spectra of authentic samples described in the literature (**2d–e**).[24]

This methodology for obtaining α,β-unsaturated esters is also general: R^1, R^2 and R^3 can be widely varied. R^1 can be aliphatic (linear, branched or cyclic) or aromatic, and substitution at the C2 position could also be changed using different esters to prepare the starting compounds **4** (Scheme 4). Interestingly, the diastereoselectivity was unaffected by changing the carboxyl ester (Table 2, entries 5 and 10) in opposition to the Wittig olefination reaction.[25]

2.3. Mechanism

The observed results and the *E*-configuration of products **1** or **2** can be explained (Scheme 5) assuming the initial metallation of the C–Cl bond of **3** or **4** by two consecutive single electron transfers from $CrCl_2$ to afford a chromium enolate like **8**. The Cr^{III} center would be coordinated to the oxygen atom of the alcohol to produce a six-membered ring. Tentatively, we assume the involvement of a chair-like transition state model **I**, with the R^1 group adopting an equatorial orientation to avoid 1,3-diaxial interactions. Elimination from **I** leads to α,β-unsaturated ketones **1** or esters **2** with total (*E*)-stereoselectivity.



Scheme 5. Proposed mechanism.

Synthesis of **1** or **2** with total stereoselection from a mixture of diastereoisomers of **3** or **4** could be also explained taking into account that after reaction of **3** or **4** with $CrCl_2$, the stereogenic C–Cl center suffers enolization. Therefore, the mixture of diastereoisomers **3** or **4** is transformed to a mixture of enantiomers **8**, which eliminates to afford a single (*E*)-stereoisomer **1** or **2**.

3. Conclusion

In conclusion, an easy, simple and general method has been developed to synthesise α,β-unsaturated ketones **1** or esters **2** in high yield and with total (*E*)-stereoselectity from readily available 2-halo-3-hydroxy ketones **3** or esters **4** and being promoted by chromium dichloride.

4. Experimental

4.1. General remarks

Reactions which required an inert atmosphere were conducted under dry nitrogen, and the glassware was oven dried (120 °C). THF was distilled from sodium/benzophenone ketyl immediately prior to use. All reagents were commercially available and were used without further purification. Silica gel for flash chromatography was purchased from Merck (230–400 mesh), and compounds were visualized on analytical thin-layer chromatograms (TLC) by UV light (254 nm). ^{1}H NMR spectra were recorded at 200, 300 or 400 MHz. ^{13}C NMR spectra and DEPT experiments were determined at 75 or 100 MHz. Chemical shifts are given in ppm relative to tetramethylsilane (TMS), which is used as an internal standard, and coupling constants *J* are reported in Hz. The diastereoisomeric excesses were obtained from ^{1}H NMR analysis and GC–MS of crude products. GC–MS and HRMS were measured at 70 eV. Only the most important IR absorptions (cm^{-1}) and the molecular ions and/or base peaks in MS are given.

4.2. General procedure for the synthesis of starting compounds 3

To a −78 °C stirred solution of the α-haloketone (9.7 mmol) in dry THF (8 mL) was added dropwise lithium diisopropylamide [prepared from MeLi (6.5 mL of 1.5 M solution in ether) and diisopropylamine (1.4 mL, 10 mmol) in THF (50 mL) at 0 °C]. After stirring for 10 min, a solution of the aldehyde (5 mmol) in dry THF (4.5 mL) was added dropwise at −78 °C and the mixture was stirred for 2 h. Then the reaction mixture was quenched with an aqueous saturated solution of NH_4Cl (20 mL). Usual workup provided the corresponding α-halo-β-hydroxy ketone **3**, which was purified by flash column chromatography on silica gel (hexane/EtOAc 10:1).

4.2.1. 2-Chloro-3-hydroxy-1-phenylheptan-1-one (3a). Data on the 50:50 mixture of diastereoisomers. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11–7.23 (m, 10H), 5.11 (d, *J*=4.3 Hz, 1H), 4.93 (d, *J*=7.9 Hz, 1H), 4.22–4.14 (m, 2H), 2.95 (s, 2H), 1.92–1.86 (m, 12H), 0.96–0.89

(m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.4 (C), 194.3 (C), 134.5 (2×C), 134.0 (CH), 133.9 (2×CH), 128.9 (4×CH), 128.7 (2×CH), 128.6 (CH), 71.6 (CH), 70.8 (CH), 60.6 (CH), 57.6 (CH), 33.2 (CH_2), 32.3 (CH_2), 27.6 (CH_2), 27.2 (CH_2), 22.3 (2×CH_2), 13.8 (CH_3), 13.7 (CH_3); MS (70 eV, EI) *m/z* (%) 205 $[M-Cl]^+$ (3), 154 (12), 123 (25), 105 (100), 78 (14), 77 (44), 51 (12), 41 (19); IR (neat): $\tilde{\nu}$=3476, 3086, 2956, 2870, 1688, 1596, 1448 cm^{-1}; R_f=0.36 (hexane/EtOAc 5:1).

4.2.2. 2-Chloro-3-hydroxy-1-phenyldecan-1-one (3b). Data on the 50:50 mixture of diastereoisomers. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01–7.45 (m, 10H), 5.09 (d, J=4.0 Hz, 1H), 4.94 (d, J=7.7 Hz, 1H), 4.25–4.18 (m, 2H), 3.32 (s, 2H), 2.01–1.15 (m, 24H), 0.89–0.85 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.4 (C), 194.2 (C), 134.5 (C), 134.2 (C), 133.9 (2×CH), 133.8 (2×CH), 128.8 (4×CH), 128.6 (2×CH), 71.5 (CH), 70.9 (CH), 60.7 (CH), 57.6 (CH), 33.5 (2×CH_2), 31.6 (2×CH_2), 29.2 (CH_2), 29.0 (CH_2), 25.4 (CH_2), 25.0 (CH_2), 22.4 (4×CH_2), 13.9 (2×CH_3); MS (70 eV, EI) *m/z* (%) 247 $[M-Cl]^+$ (5), 158 (5), 154 (16), 123 (20), 106 (8), 105 (100), 78 (13), 77 (38), 43 (21), 41 (22); IR (neat): $\tilde{\nu}$=3387, 3063, 2951, 2923, 2855, 1689, 1596, 1581, 1464, 1449 cm^{-1}; R_f=0.45 (hexane/EtOAc 5:1).

4.2.3. 2-Chloro-3-cyclohexyl-3-hydroxy-1-phenylpropan-1-one (3c). White solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.00–7.26 (m, 5H), 5.32 (d, J=2.8 Hz, 1H), 3.89 (ddd, J=7.9, 4.8, 2.8 Hz, 1H), 3.06 (d, J=4.8 Hz, 1H), 2.10–2.04 (m, 1H), 1.85–1.53 (m, 5H), 1.48–0.84 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.5 (C), 134.1 (C), 134.0 (CH), 128.8 (2×CH), 128.7 (2×CH), 75.0 (CH), 59.1 (CH), 40.1 (CH), 28.8 (CH_2), 28.5 (CH_2), 26.0 (CH_2), 25.7 (CH_2), 25.5 (CH_2); MS (70 eV, EI) *m/z* (%) 231 $[M-Cl]^+$ (9), 156 (7), 154 (20), 147 (19), 123 (9), 105 (100), 83 (12), 82 (13), 78 (25), 77 (72), 73 (28), 55 (41), 51 (20); IR (neat): $\tilde{\nu}$=3507, 3058, 2923, 2852, 1683, 1596, 1580, 1448, 1392, 1265, 1208, 1071 cm^{-1}; R_f=0.47 (hexane/EtOAc 5:1).

4.2.4. 2-Chloro-3-hydroxy-1,3-diphenylpropan-1-one (3d). Data on the 65:55 mixture of diastereoisomers. White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05–7.28 (m, 20H), 5.37 (d, J=5.7 Hz, 1H), 5.31 (d, J=5.7 Hz, 1H), 5.30 (d, J=8.5 Hz, 1H), 5.20 (d, J=8.5 Hz, 1H), 3.70 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.3 (C), 194.0 (C), 139.1 (C), 138.5 (C), 134.5 (2×C), 134.0 (CH), 128.9 (CH), 128.7 (4×CH), 128.1 (2×CH), 128.4 (4×CH), 128.3 (4×CH), 128.2 (2×CH), 127.1 (CH), 126.7 (CH), 74.5 (CH), 73.2 (CH), 61.3 (CH), 57.4 (CH); IR (neat): $\tilde{\nu}$=3504, 3087, 3032, 1964, 1903, 1695, 1595, 1580, 1453, 1307, 1062 cm^{-1}; R_f=0.34 (hexane/EtOAc 5:1).

4.2.5. 2-Chloro-3-hydroxy-5-methyl-1-phenylhexan-1-one (3e). Data on the 50:50 mixture of diastereoisomers. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61–7.45 (m, 10H), 7.99 (d, J=7.9 Hz, 2H), 4.91 (d, J=7.9 Hz, 2H), 4.29 (s, 2H), 2.14–1.54 (m, 6H), 0.94 (d, J=6.9 Hz, 6H), 0.89 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.0 (C), 196.9 (C), 137.1 (2×C), 136.6 (2×CH), 131.5 (4×CH), 131.3 (4×CH), 72.7 (CH), 71.5 (CH), 63.5 (CH), 60.7 (CH), 45.0 (CH_2), 44.3 (CH_2), 26.8 (CH), 26.2 (CH), 25.8 (2×CH_3), 24.2 (CH_3), 23.8 (CH_3); R_f=0.37 (hexane/EtOAc 5:1).

4.2.6. 2-Chloro-3-hydroxy-1,4-diphenylpentan-1-one (3f). White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.95–7.31 (m, 10H), 5.03 (s, 1H), 4.31 (dd, J=8.2, 5.9 Hz, 1H), 3.58 (d, J=5.9 Hz, 1H), 3.31–3.08 (m, 1H), 1.50 (d, J=6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.3 (C), 142.7 (C), 133.9 (CH), 133.7 (C), 128.8 (CH), 128.7 (2×CH), 128.6 (2×CH), 128.1 (2×CH), 127.6 (CH), 127.2 (CH), 75.5 (CH), 60.1 (CH), 43.1 (CH), 17.9 (CH_3); R_f=0.42 (hexane/EtOAc 5:1).

4.2.7. 6-Chloro-7-hydroxyundec-5-one (3g). Data on the 60:40 mixture of diastereoisomers. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.25 (d, J=3.4 Hz, 2H), 4.13–4.08 (m, 4H), 2.75–2.66 (m, 4H), 1.65–1.27 (m, 20H), 0.93 (t, J=7.2 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.3 (C), 205.9 (C), 72.1 (CH), 71.4 (CH), 67.7 (CH), 64.1 (CH), 40.0 (CH_2), 39.9 (CH_2), 33.5 (2×CH_2), 32.6 (2×CH_2), 27.5 (CH_2), 27.2 (CH_2), 25.3 (2×CH_2), 22.3 (2×CH_2), 22.0 (2×CH_3), 13.7 (2×CH_3); IR (neat): $\tilde{\nu}$=3427, 2958, 2932, 2872, 1711, 1466, 1379 cm^{-1}; R_f=0.23 (hexane/EtOAc 10:1).

4.2.8. 2-Chloro-1-hydroxy-1-phenylheptan-3-one (3h). Data on the 50:50 mixture of diastereoisomers. Yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41–7.32 (m, 10H), 5.16 (d, J=5.3 Hz, 1H), 5.01 (d, J=8.2 Hz, 1H), 4.44 (d, J=5.3 Hz, 1H), 4.35 (d, J=8.2 Hz, 1H), 3.12 (s, 2H), 2.67–2.30 (m, 4H), 2.30–1.66 (m, 8H), 0.91 (t, J=6.9 Hz, 3H), 0.86 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.5 (C), 205.2 (C), 139.0 (C), 138.7 (C), 128.4 (CH), 128.3 (2×CH), 128.2 (4×CH), 126.8 (2×CH), 126.4 (CH), 74.7 (CH), 73.6 (CH), 67.5 (CH), 63.4 (CH), 40.7 (CH_2), 40.1 (CH_2), 25.2 (CH_2), 25.0 (CH_2), 21.8 (CH_2), 21.7 (CH_2), 13.6 (CH_3), 13.5 (CH_3); IR (neat): $\tilde{\nu}$=3460, 3088, 3033, 1714, 1604, 1495, 1454, 1380, 1267, 1050 cm^{-1}; R_f=0.30 (hexane/EtOAc 5:1).

4.2.9. (*R,*R**)-4-Chloro-5-hydroxy-2,2-dimethylnonan-3-one (3i).** Yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.38 (d, J=8.5 Hz, 1H), 4.03 (dt, J=8.5, 2.3 Hz, 1H), 3.28 (s, 1H), 1.59–1.31 (m, 6H), 1.23 (s, 9H), 0.92 (t, J=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 210.6 (C), 72.0 (CH), 55.0 (CH), 44.6 (C), 32.3 (CH_2), 27.2 (CH_2), 26.2 (3×CH_3), 22.4 (CH_2), 13.9 (CH_3); IR (neat): $\tilde{\nu}$=3512, 2986, 2913, 2857, 1715, 1478, 1369, 1096 cm^{-1}; R_f=0.37 (hexane/EtOAc 5:1).

4.2.10. 3-Chloro-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (3j). Orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (d, J=6.9 Hz, 2H), 7.01 (d, J=6.9 Hz, 2H), 5.99 (d, J=7.9 Hz, 2H), 3.89 (s, 3H), 3.28 (s, 1H), 1.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.0 (C), 164.5 (C), 131.9 (2×CH), 129.6 (C), 114.1 (2×CH), 78.4 (CH), 70.0 (CH), 55.4 (CH_3), 22.7 (CH_3); R_f=0.44 (hexane/EtOAc 5:1).

4.3. General procedure for the synthesis of (*E*)-α,β-unsaturated ketones (1) by using $CrCl_2$

To a stirred suspension of $CrCl_2$ (3 equiv) in THF (10 mL) was added a solution of the corresponding 2-halo-3-hydroxy

ketone **3** (1 equiv). After stirring at reflux temperature for 4 h, the reaction was quenched with HCl 1 N (5 mL) and extracted with diethyl ether (3×10 mL). The combined extracts were washed with water, dried over Na_2SO_4 and concentrated under reduced pressure. When it was necessary, purification by flash chromatography on silica gel (hexane/EtOAc 10:1) afforded the α,β-unsaturated ketones **1**.

4.4. General procedure for the synthesis of (*E*)-α,β-unsaturated ketones (1) by using SmI_2

Over a solution of the starting α-chloro-β-hydroxy ketone **3** (0.4 mmol) in dry THF (2 mL) a solution of samarium diiodide [prepared from 0.069 g of Sm (0.4 mmol), 5 mL of dry THF and 0.032 mL of CH_2I_2] was added dropwise at −25 °C. The reaction mixture was stirred at the same temperature over 2 h and then heated at reflux for one additional hour (the colour changed from yellow to orange). The reaction mixture was quenched with 5 mL of 0.1 M HCl and the usual workup gave the crude α,β-unsaturated ketone. Purification by flash column chromatography over silica or by distillation afforded the pure compound **1**.

4.5. General procedure for the synthesis of (*E*)-α,β-unsaturated ketones (1) by using SmI_3

0.4 mmol of the starting ketone were treated with a solution of 0.4 mmol of samarium triiodide (0.069 g of Sm, 5 mL of dry THF and 0.150 g of I_2) at −25 °C during 2 h and later heated at reflux by one additional hour. The reaction was quenched with 5 mL of 0.1 M HCl, extracted with dichloromethane and concentrated. Purification by flash column chromatography or by distillation yielded the pure enone **1**.

4.5.1. (*E*)-1-Phenylhept-2-en-1-one (1a). Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93–7.41 (m, 5H), 7.06 (dt, *J*=15.4, 6.8 Hz, 1H), 6.86 (d, *J*=15.4 Hz, 1H), 2.29 (q, *J*=6.8 Hz, 2H), 1.70–1.19 (m, 4H), 0.92 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.8 (C), 150.1 (CH), 137.9 (C), 132.5 (CH), 125.8 (CH), 128.4 (4×CH), 32.4 (CH_2), 30.1 (CH_2), 22.2 (CH_2), 13.7 (CH_3); MS (70 eV, EI) *m*/*z* (%) 188 $[M]^+$ (15), 159 (14), 145 (14), 131 (14), 115 (18), 105 (100), 91 (18), 77 (85), 55 (42), 51 (37), 43 (22), 41 (40); IR (neat): $\tilde{\nu}$=3085, 3059, 3028, 2957, 2930, 2871, 1725, 1670, 1620, 1597, 1447, 1344, 1282, 1003 cm^{-1}; R_f=0.34 (hexane/EtOAc 10:1). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.17; H, 8.46.

4.5.2. (*E*)-1-Phenyldec-2-en-1-one (1b). Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96–7.38 (m, 5H), 7.08 (dt, *J*=15.4, 6.7 Hz, 1H), 6.88 (d, *J*=15.4 Hz, 1H), 2.32 (q, *J*=6.7 Hz, 2H), 1.65–1.21 (m, 10H), 0.89 (t, *J*=6.8 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 190.7 (C), 150.0 (CH), 137.8 (C), 132.4 (CH), 128.4 (4×CH), 125.6 (CH), 32.7 (CH_2), 31.6 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 28.0 (CH_2), 22.5 (CH_2), 13.9 (CH_3); MS (70 eV, EI) *m*/*z* (%) 230 $[M]^+$ (3), 159 (15), 145 (13), 133 (19), 120 (3), 105 (100), 91 (16), 77 (69), 73 (28), 55 (33), 43 (51), 41 (65); HRMS (70 eV) calcd for $C_{16}H_{22}O$ 230.1671, found 230.1679; IR (neat): $\tilde{\nu}$=3059, 2956, 2927, 2855, 1672, 1622, 1463, 1448 cm^{-1}; R_f=0.34 (hexane/EtOAc 10:1). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.65; H, 9.75.

4.5.3. (*E*)-3-Cyclohexyl-1-phenylpropenone (1c). Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93–7.26 (m, 5H), 7.01 (dd, *J*=15.4, 6.7 Hz, 1H), 6.82 (dd, *J*=15.4, 1.1 Hz, 1H), 2.26–2.22 (m, 1H), 1.85–1.70 (m, 5H), 1.36–1.19 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.3 (C), 154.9 (CH), 138.0 (C), 132.5 (CH), 128.4 (4×CH), 123.2 (CH), 41.0 (CH), 31.7 (2×CH_2), 25.8 (CH_2), 25.7 (2×CH_2); MS (70 eV, EI) *m*/*z* (%) 214 $[M]^+$ (13), 157.2 (7), 120 (9), 115 (9), 105 (100), 91 (9), 79 (12), 77 (60), 67 (14), 55 (21), 51 (20); HRMS (70 eV) calcd for $C_{15}H_{18}O$ 214.1358, found 214.1368; IR (neat): $\tilde{\nu}$=3084, 3057, 3025, 2996, 2925, 2851, 1725, 1665, 1614, 1578, 1446, 1336, 1016, 984 cm^{-1}; R_f=0.40 (hexane/EtOAc 10:1). Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 83.67; H, 8.39.

4.5.4. (*E*)-1,3-Diphenylpropenone (1d). White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08–7.28 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.3 (C), 144.6 (CH), 137.9 (C), 134.6 (C), 132.6 (CH), 130.4 (CH), 128.8 (2×CH), 128.4 (2×CH), 128.3 (4×CH), 121.7 (CH); MS (70 eV, EI) *m*/*z* (%) 208 $[M]^+$ (25), 207 (34), 179 (9), 165 (5), 131 (16), 103 (23), 102 (19), 77 (100), 51 (51), 50 (19). Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.62; H, 5.73.

4.5.5. (*E*)-5-Methyl-1-phenylhex-2-en-1-one (1e). Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96–7.11 (m, 5H), 7.06 (dt, *J*=15.1, 7.0 Hz, 1H), 6.88 (d, *J*=15.1 Hz, 1H), 2.23 (t, *J*=7.0 Hz, 2H), 2.18–1.80 (m, 1H), 0.98 (d, *J*=6.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.7 (C), 148.8 (CH), 137.9 (C), 132.5 (CH), 128.4 (4×CH), 126.9 (CH), 42.0 (CH_2), 27.9 (CH), 22.4 (2×CH_3); MS (70 eV, EI) *m*/*z* (%) 188 $[M]^+$ (5), 158 (120), 77 (30); IR (neat): $\tilde{\nu}$=3064, 2957, 2870, 1687, 1597, 1449, 1251 cm^{-1}; R_f=0.32 (hexane/EtOAc 10:1). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.01; H, 8.46.

4.5.6. (*E*)-1,4-Diphenylpent-2-en-1-one (1f). Yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96 (dd, *J*=6.9, 1.5 Hz, 2H), 7.58–7.24 (m, 9H), 6.91 (dd, *J*=15.5, 1.4 Hz, 1H), 3.79 (quint., *J*=7.0 Hz, 1H), 1.57 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.9 (C), 152.9 (CH), 143.3 (C), 137.8 (C), 132.6 (CH), 128.6 (2×CH), 128.4 (4×CH), 127.3 (2×CH), 126.7 (CH), 124.4 (CH), 42.5 (CH), 20.4 (CH_3); MS (70 eV, EI) *m*/*z* (%) 236 $[M]^+$ (19), 221 (8), 131 (27), 105 (100), 77 (46); IR (neat): $\tilde{\nu}$=3027, 2968, 1669, 1619, 1448, 1290 cm^{-1}; R_f=0.57 (hexane/EtOAc 3:1). Anal. Calcd for $C_{17}H_{16}O$: C, 86.40; H, 6.82. Found: C, 86.49; H, 6.73.

4.5.7. (*E*)-Undec-6-en-5-one (1g). Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.80 (dt, *J*=14.9, 6.9 Hz, 1H), 6.06 (d, *J*=14.9 Hz, 1H), 2.50 (t, *J*=7.1 Hz, 2H), 2.19 (q, *J*=7.1 Hz, 2H), 1.59–1.28 (m, 8H), 0.89 (t, *J*=7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.9 (C), 147.2 (CH), 130.2 (CH), 39.7 (CH_2), 32.0 (CH_2), 30.1 (CH_2), 26.3 (CH_2), 22.3 (CH_2), 21.9 (CH_2), 13.8 (CH_3), 13.7 (CH_3); MS (70 eV, EI) *m*/*z* (%) 168 $[M]^+$ (<1), 126 (26), 111 (100), 83 (7), 55 (94), 29 (17); IR (neat): $\tilde{\nu}$=3024, 2961, 2869, 1700, 1676, 1633, 1465, 1261 cm^{-1}; R_f=0.49 (hexane/EtOAc 5:1).

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.73; H, 11.86.

4.5.8. (*E*)-1-Phenylhept-1-en-3-one (1h). Yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.70–7.37 (m, 6H), 6.76 (d, J=16.2 Hz, 1H), 2.68 (t, J=7.4 Hz, 2H), 1.76–1.27 (m, 4H), 0.92 (t, J=7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 200.6 (C), 142.2 (CH), 134.5 (C), 130.3 (CH), 128.8 (CH), 128.2 (2×CH), 126.2 (2×CH), 40.6 (CH_2), 26.4 (CH_2), 22.4 (CH_2), 13.8 (CH_3); MS (70 eV, EI) *m*/*z* (%) 188 $[M]^+$ (7), 146 (41), 131 (100), 103 (46), 77 (27), 51 (8); HRMS (70 eV) calcd for $C_{13}H_{16}O$ 188.1201, found 188.1198; IR (neat): $\tilde{\nu}$=3021, 2937, 2865, 1686, 1620, 1500, 1181, 1069 cm^{-1}; R_f=0.47 (hexane/EtOAc 5:1). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.03; H, 8.51.

4.5.9. (*E*)-2,2-Dimethylnon-4-en-3-one (1i). Pale orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.94 (dt, J=15.2, 6.8 Hz, 1H), 6.47 (d, J=15.2 Hz, 1H), 2.18 (q, J=7.1 Hz, 2H), 1.47–1.21 (m, 4H), 1.15 (s, 9H), 0.91 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.4 (C), 147.6 (CH), 124.0 (CH), 42.7 (C), 32.1 (CH_2), 30.2 (CH_2), 26.1 (3×CH_3), 22.2 (CH_2), 13.8 (CH_3); MS (70 eV, EI) *m*/*z* (%) 168 $[M]^+$ (5), 111 (100), 83 (8), 57 (30); IR (neat): $\tilde{\nu}$=2958, 2929, 2871, 1705, 1624, 1458, 1364, 1066, 1003, 720 cm^{-1}; R_f=0.47 (hexane/EtOAc 10:1). Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.75; H, 11.86.

4.5.10. (*E*)-4-(4-Methoxyphenyl)but-3-en-2-one (1j). Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J=11.5 Hz, 1H), 7.43 (d, J=11.2 Hz, 2H), 6.84 (d, J=11.2 Hz, 2H), 6.54 (d, J=11.5 Hz, 1H), 3.77 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.6 (C), 161.6 (C), 143.4 (CH), 129.9 (2×CH), 126.9 (C), 124.9 (CH), 114.4 (2×CH), 55.3 (CH_3), 27.3 (CH_3); MS (70 eV, EI) *m*/*z* (%) 176 $[M]^+$ (52), 161 (100), 145 (8), 133 (48), 118 (16), 89 (17), 77 (14); IR (neat): $\tilde{\nu}$=2959, 2918, 2849, 1664, 1602, 1512, 1250 cm^{-1}; R_f=0.48 (hexane/EtOAc 1:1). Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 75.09; H, 6.77.

4.6. General procedure for the synthesis of starting compounds 4

To a −78 °C stirred solution of the α-haloester (9.7 mmol) in dry THF (8 mL) was added dropwise lithium diisopropylamide [prepared from MeLi (6.5 mL of 1.5 M solution in ether) and diisopropylamine (1.4 mL, 10 mmol) in THF (50 mL) at 0 °C]. After stirring for 10 min, a solution of the aldehyde (5 mmol) in dry THF (4.5 mL) was added dropwise at −78 °C and the mixture was stirred for 2 h. Then the reaction mixture was quenched with an aqueous saturated solution of NH_4Cl (20 mL). Usual workup provided the corresponding α-halo-β-hydroxyester **4**, which was purified by flash column chromatography on silica gel (hexane/EtOAc 10:1).

4.6.1. Methyl 2-chloro-3-hydroxydecanoate (4a). Data on the 50:50 mixture of diastereoisomers. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.27 (d, J=3.9 Hz, 1H), 4.14 (d, J=3.9 Hz, 1H), 4.12–3.90 (m, 2H), 3.88–3.75 (m, 2H), 3.73 (s, 3H), 3.71 (s, 3H), 1.66–1.21 (m, 24H), 0.80 (t, J=6.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2 (C), 168.9 (C), 72.4 (CH), 71.7 (CH), 61.9 (CH), 59.4 (CH), 52.9 (CH_3), 52.7 (CH_3), 31.9 (CH_2), 31.5 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.7 (CH_2), 25.2 (CH_2), 24.9 (2×CH_2), 24.5 (2×CH_2), 22.4 (2×CH_2), 13.8 (2×CH_3); IR (neat): $\tilde{\nu}$=3452, 1754 cm^{-1}; R_f=0.30 (hexane/EtOAc 5:1).

4.6.2. Methyl 2-chloro-3-(4-chlorophenyl)-3-hydroxypropanoate (4b). Data on the 50:50 mixture of diastereoisomers. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33–7.26 (m, 8H), 5.07 (d, J=6.0 Hz, 1H), 4.95 (d, J=6.0 Hz, 1H), 4.46 (s, 2H), 4.42 (dd, J=6.0, 1.5 Hz, 1H), 4.33 (dd, J=6.0, 1.5 Hz, 1H), 3.76 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0 (C), 168.1 (C), 137.1 (C), 136.7 (C), 134.0 (2×C), 128.3 (CH), 128.2 (2×CH), 128.1 (4×CH), 127.7 (CH), 74.1 (CH), 73.4 (CH), 62.2 (CH), 58.8 (CH), 53.0 (CH_3), 52.8 (CH_3); IR (neat): $\tilde{\nu}$=3468, 1744, 1493, 1285 cm^{-1}; R_f=0.40 (hexane/EtOAc 5:1).

4.6.3. Methyl 2-chloro-3-hydroxy-4-phenylpentanoate (4c). Data on the 50:50 mixture of diastereoisomers. Yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.50–7.20 (m, 10H), 4.24 (dd, J=1.4 Hz, 2H), 4.14–4.02 (m, 4H), 3.78 (s, 3H), 3.58 (s, 3H), 2.851 (s, 2H), 1.45 (d, J=6.9 Hz, 3H), 1.36 (d, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1 (C), 169.0 (C), 142.8 (C), 142.3 (C), 128.6 (CH), 128.5 (2×CH), 128.2 (2×CH), 128.0 (2×CH), 127.6 (2×CH), 127.3 (CH), 76.8 (CH), 76.3 (CH), 60.7 (CH), 57.1 (CH), 52.9 (CH_3), 52.7 (CH_3), 43.0 (CH), 40.9 (CH), 18.0 (CH_3), 14.5 (CH_3); IR (neat): $\tilde{\nu}$=2950, 1717, 1632, 1168, 1039 cm^{-1}; R_f=0.32 (hexane/EtOAc 5:1).

4.6.4. Ethyl 2-chloro-3-hydroxy-2-methyldecanoate (4d). Data on the 60:40 mixture of diastereoisomers. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.25 (q, J=7.1 Hz, 2H), 4.24 (q, J=7.1 Hz, 2H), 3.98 (s, 1H), 3.96 (s, 1H), 2.61 (m, 2H), 1.71 (s, 3H), 1.70 (s, 3H), 1.67–1.27 (m, 30H), 0.86 (t, J=7.1 Hz, 3H), 0.79 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.9 (C), 170.5 (C), 75.9 (CH), 75.6 (CH), 73.6 (C), 71.1 (C), 62.2 (2×CH_2), 31.6 (CH_2), 31.5 (CH_2), 31.0 (4×CH_2), 29.2 (4×CH_2), 29.1 (CH_2), 26.2 (CH_2), 22.5 (2×CH_3), 22.2 (2×CH_3), 13.9 (CH_3), 13.8 (CH_3); IR (neat): $\tilde{\nu}$=3425, 1741 cm^{-1}; R_f=0.26 (hexane/EtOAc 10:1).

4.6.5. Ethyl 2-chloro-3-cyclohexyl-3-hydroxy-2-methylpropanoate (4e). Data on the 50:50 mixture of diastereoisomers. White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.14 (q, J=7.2 Hz, 4H), 3.84–3.76 (m, 2H), 2.90 (s, 2H), 1.93–1.09 (m, 22H), 1.88 (s, 6H), 1.21 (t, J=7.2 Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.9 (C), 170.5 (C), 79.3 (CH), 78.7 (CH), 73.6 (C), 71.9 (C), 62.0 (CH_2), 61.9 (CH_2), 40.7 (CH), 40.3 (CH), 31.0 (CH_2), 30.5 (CH_2), 30.2 (CH_2), 28.4 (CH_2), 27.9 (CH_2), 26.2 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 25.1 (CH_2), 24.9 (CH_2), 21.8 (CH_3), 21.2 (CH_3), 13.6 (CH_3), 13.3 (CH_3); R_f=0.31 (hexane/EtOAc 10:1).

4.6.6. Ethyl 2-chloro-3-hydroxy-2-methyl-3-phenylpropanoate (4f). Pale yellow solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.46–7.34 (m, 5H), 5.22 (s, 1H), 4.29 (q, J=7.1 Hz, 2H), 3.22 (s, 1H), 1.66 (s, 3H), 1.32 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8 (C), 137.4 (C), 128.3 (CH), 128.1 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 77.6 (CH), 69.4 (C), 62.4 (CH_2), 21.6 (CH_3), 13.8

(CH_3); IR (neat): $\tilde{\nu}$=2994, 1724, 1454 cm^{-1}; R_f=0.43 (hexane/EtOAc 5:1).

4.6.7. Ethyl 2-chloro-3-hydroxy-2-methyl-3-(4-methoxyphenyl)propanoate (4g). Data on the 75:25 mixture of diastereoisomers. Pale orange oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.37–7.28 (m, 4H), 6.89–6.80 (m, 4H), 5.21 (s, 1H), 5.15 (s, 1H), 4.27 (q, J=7.2 Hz, 2H), 4.26 (q, J=7.2 Hz, 2H), 3.78 (s, 3H), 3.73 (s, 3H), 3.29 (m, 2H), 1.64 (s, 3H), 1.57 (s, 3H), 1.31 (t, J=7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8 (C), 170.4 (C), 159.4 (C), 159.3 (C), 129.8 (C), 129.4 (2×CH), 129.2 (2×CH), 128.9 (C), 113.1 (2×CH), 112.9 (2×CH), 77.0 (2×CH), 73.5 (C), 69.8 (C), 62.3 (CH_2), 62.1 (CH_2), 55.0 (2×CH_3), 22.6 (CH_3), 21.4 (CH_3), 13.7 (2×CH_3); IR (neat): $\tilde{\nu}$=3490, 1737 cm^{-1}; R_f=0.33 (hexane/EtOAc 5:1).

4.6.8. Ethyl 2-bromo-3-hydroxy-2-hexyl-3-phenylpropanoate (4h). Data on the 50:50 mixture of diastereoisomers. Yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–7.33 (m, 10H), 5.09 (s, 2H), 4.25 (q, J=7.1 Hz, 4H), 3.60 (s, 2H), 2.06–1.76 (m, 4H), 1.56–1.20 (m, 22H), 0.90 (t, J=7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.7 (C), 169.2 (C), 138.3 (C), 137.8 (C), 127.8 (2×CH), 127.7 (2×CH), 127.6 (4×CH), 127.1 (2×CH), 78.1 (CH), 77.6 (CH), 75.6 (C), 73.8 (C), 62.0 (CH_2), 61.7 (CH_2), 37.6 (CH_2), 37.0 (CH_2), 31.4 (CH_2), 31.1 (CH_2), 31.0 (CH_2), 28.8 (CH_2), 28.6 (CH_2), 25.8 (CH_2), 25.5 (CH_2), 22.1 (CH_2), 13.6 (CH_3), 13.5 (CH_3), 13.4 (CH_3), 13.3 (CH_3); IR (neat): $\tilde{\nu}$=3503, 2956, 1734, 1717 cm^{-1}; R_f=0.32 (hexane/EtOAc 5:1).

4.6.9. Ethyl 2-bromo-3-hydroxy-2-pentyl-3-phenylpropanoate (4i). Yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–7.36 (m, 5H), 5.12 (s, 1H), 4.30 (q, J=7.1 Hz, 2H), 3.39 (s, 1H), 2.06–1.83 (m, 2H), 1.79–1.24 (m, 9H), 0.90 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.1 (C), 137.8 (C), 128.3 (CH), 128.0 (CH), 127.9 (2×CH), 127.6 (CH), 77.6 (CH), 75.9 (C), 62.5 (CH_2), 37.3 (CH_2), 31.4 (CH_2), 25.5 (CH_2), 22.1 (CH_2), 13.8 (CH_3), 13.7 (CH_3); IR (neat): $\tilde{\nu}$=3503, 2931, 1734, 1455 cm^{-1}; R_f=0.31 (hexane/EtOAc 5:1).

4.6.10. Isopropyl 2-chloro-3-cyclohexyl-3-hydroxy-2-methylpropanoate (4j). Data on the 65:55 mixture of diastereoisomers. Yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ 5.07 (apparent quint., J=6.1 Hz, 2H), 3.81 (d, J=4.7 Hz, 1H), 3.75 (d, J=4.7 Hz, 1H), 2.58 (s, 2H), 1.75 (s, 3H), 1.71 (s, 3H), 1.91–1.18 (m, 22H), 1.30 (d, J=6.1 Hz, 6H), 1.27 (d, J=6.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4 (C), 170.0 (C), 79.4 (CH), 78.8 (CH), 73.8 (C), 72.2 (C), 69.9 (CH), 69.7 (CH), 40.7 (CH), 40.3 (CH), 31.2 (CH_2), 30.8 (CH_2), 28.4 (CH_2), 26.6 (CH_2), 26.3 (2×CH_2), 26.0 (2×CH_2), 25.9 (2×CH_2), 22.4 (2×CH_3), 21.9 (CH_3), 21.5 (CH_3), 21.2 (CH_3), 21.1 (CH_3); IR (neat): $\tilde{\nu}$=3499, 1732, 1450, 1376, 1266 cm^{-1}; R_f=0.37 (hexane/EtOAc 5:1).

4.7. General procedure for the synthesis of α,β-unsaturated esters 2

To a stirred solution of the corresponding β-hydroxyester α-halogenated **4** (0.4 mmol) in dry THF (5 mL) was added $CrCl_2$ (0.15 g, 1.2 mmol). After 4 h at reflux the reaction mixture was quenched with water. Usual workup and filtration through a pad of Celite provided α,β-unsaturated esters **2**, which were purified by flash column chromatography on silica gel (hexane/EtOAc 15:1).

4.7.1. (*E*)-Methyl dec-2-enoate (2a). Yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ 6.96 (dt, J=15.4, 7.0 Hz, 1H), 5.81 (dt, J=15.4, 1.3 Hz, 1H), 3.71 (s, 3H), 2.23–2.14 (m, 2H), 1.46–1.26 (m, 10H), 0.87 (t, J=6.8 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 167.1 (C), 149.8 (CH), 120.7 (CH), 51.3 (CH_3), 32.1 (CH_2), 31.6 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 27.9 (CH_2), 22.5 (CH_2), 14.0 (CH_3); MS (70 eV, EI) *m*/*z* (%) 184 $[M]^+$ (<1), 153 (28), 87 (100); IR (neat): $\tilde{\nu}$=2928, 1728, 1651 cm^{-1}; HRMS (70 eV) calcd for $C_{11}H_{20}O_2$ 184.2753, found 184.1463; R_f=0.50 (hexane/EtOAc 10:1). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.81; H, 10.85.

4.7.2. (*E*)-Methyl 3-(4-chlorophenyl)prop-2-enoate (2b). Yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, J=16.1 Hz, 1H), 7.50–7.48 (AB system, J=6.5 Hz, 4H), 6.45 (d, J=16.1 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1 (C), 143.3 (CH), 136.1 (C), 132.8 (C), 129.1 (2×CH), 129.0 (2×CH), 118.3 (CH), 51.7 (CH_3); IR (neat): $\tilde{\nu}$=2283, 1728, 1168, 937, 821, 731 cm^{-1}; R_f=0.51 (hexane/EtOAc 3:1). Anal. Calcd for $C_{10}H_9ClO_2$: C, 61.08; H, 4.61. Found: C, 61.28; H, 4.49.

4.7.3. (*E*)-Methyl 4-phenylpent-2-enoate (2c). Yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ 7.50–7.17 (m, 5H), 7.13 (d, J=15.6 Hz, 1H), 5.83 (dd, J=15.6, 1.6 Hz, 1H), 3.78 (s, 3H), 3.67–3.57 (q, J=7.0 Hz, 1H), 1.44 (d, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0 (C), 152.8 (CH), 143.1 (C), 129.0 (2×CH), 127.6 (2×CH), 127.2 (CH), 119.5 (CH), 52.8 (CH_3), 41.9 (CH), 20.0 (CH_3); MS (70 eV, EI) *m*/*z* (%) 190 $[M]^+$ (21), 175 (5), 131 (100), 115 (74), 91 (46), 77 (23); R_f=0.53 (hexane/EtOAc 5:1). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.87; H, 7.31.

4.7.4. (*E*)-Ethyl 2-methyldec-2-enoate (2d). Yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 6.81–6.72 (m, 1H), 4.20 (q, J=7.2 Hz, 2H), 2.21–2.11 (m, 2H), 1.84 (s, 3H), 1.75–1.25 (m, 13H), 0.87 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.3 (C), 142.4 (CH), 127.5 (C), 60.3 (CH_2), 31.7 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 28.6 (CH_2), 28.5 (CH_2), 22.5 (CH_2), 14.2 (CH_3), 14.0 (CH_3), 12.2 (CH_3); MS (70 eV, EI) *m*/*z* (%) 212 $[M]^+$ (19), 167 (80), 113 (73); IR (neat): $\tilde{\nu}$=2928, 1728, 1651 cm^{-1}; R_f=0.50 (hexane/EtOAc 10:1). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.76; H, 11.24.

4.7.5. (*E*)-Ethyl 3-cyclohexyl-2-methylpropenoate (2e). White solid. ^1H NMR (300 MHz, $CDCl_3$): δ 6.57 (d, J=9.6 Hz, 1H), 4.17 (q, J=7.2 Hz, 2H), 2.45–2.25 (m, 1H), 1.82 (s, 3H), 1.83–1.05 (m, 10H), 1.28 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.5 (C), 147.2 (CH), 125.8 (C), 60.3 (CH_2), 37.6 (CH), 31.8 (2×CH_2), 25.8 (CH_2), 25.5 (2×CH_2), 14.2 (CH_3), 12.3 (CH_3); MS (70 eV, EI) *m*/*z* (%) 196 $[M]^+$ (30), 151 (34), 123 (10); IR (neat): $\tilde{\nu}$=2926, 1709, 1649, 1381 cm^{-1}; R_f=0.54 (hexane/EtOAc 10:1). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.48; H, 10.15.

4.7.6. (*E*)-Ethyl 2-methyl-3-phenylprop-2-enoate (2f). Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.69–7.26 (m, 5H), 4.23 (q, J=7.0 Hz, 2H), 2.14 (s, 3H), 1.30 (t, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.6 (C), 138.6 (CH), 135.9 (C), 129.5 (2×CH), 128.3 (C), 128.1 (3×CH), 60.8 (CH_2), 14.2 (CH_3), 14.0 (CH_3); MS (70 eV, EI) *m/z* (%) 190 $[M]^+$ (29), 115 (100), 145 (40), 91 (40); IR (neat): $\tilde{\nu}$=2927, 1708, 1638, 764 cm^{-1}; R_f=0.61 (hexane/EtOAc 3:1). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.87; H, 7.53.

4.7.7. (*E*)-Ethyl 2-methyl-3-(4-methoxyphenyl)propenoate (2g). Orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.37 (d, J=8.3 Hz, 2H), 6.89 (d, J=8.3 Hz, 2H), 4.25 (q, J=7.1 Hz, 2H), 3.80 (s, 3H), 2.12 (s, 3H), 1.33 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.8 (C), 159.4 (C), 138.2 (CH), 131.2 (2×CH), 128.3 (C), 126.1 (C), 113.6 (2×CH), 60.6 (CH_2), 55.0 (CH_3), 14.2 (CH_3), 13.9 (CH_3); MS (70 eV, EI) *m/z* (%) 220 $[M]^+$ (100), 191 (32), 175 (85), 147 (83), 131 (72), 91 (75), 77 (59); IR (neat): $\tilde{\nu}$= 2975, 1702, 1605 cm^{-1}; R_f=0.43 (hexane/EtOAc 5:1). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.02; H, 7.25.

4.7.8. (*E*)-Ethyl 2-hexyl-3-phenylprop-2-enoate (2h). Yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.41–7.36 (m, 5H), 4.33 (q, J=7.2 Hz, 2H), 2.54 (t, J= 7.2 Hz, 3H), 1.60–0.90 (m, 10H), 1.37 (t, J=6.9 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 168.4 (C), 138.3 (CH), 135.8 (C), 133.9 (C), 129.0 (CH), 128.3 (3×CH), 128.0 (CH), 60.6 (CH_2), 31.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 27.4 (CH_2), 22.5 (CH_2), 14.2 (CH_3), 13.9 (CH_3); MS (70 eV, EI) *m/z* (%) 260 $[M]^+$ (33), 144 (30), 172 (29), 77 (26); IR (neat): $\tilde{\nu}$= 2957, 2858, 1709, 1630 cm^{-1}; R_f=0.59 (hexane/EtOAc 5:1). Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.60; H, 9.13.

4.7.9. (*E*)-Ethyl 2-penthyl-3-phenylprop-2-enoate (2i). Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (s, 1H), 7.37–7.26 (m, 5H), 4.33 (q, J=7.2 Hz, 2H), 1.72–1.37 (m, 8H), 1.33 (t, J=7.2 Hz, 3H), 0.91 (t, J=10.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.4 (C), 138.3 (CH), 135.8 (C), 133.9 (C), 129.1 (2×CH), 128.3 (2×CH), 128.1 (CH), 60.4 (CH_2), 31.8 (CH_2), 28.9 (CH_2), 27.4 (CH_2), 22.3 (CH_2), 14.2 (CH_3), 13.9 (CH_3); MS (70 eV, EI) *m/z* (%) 246 $[M]^+$ (35), 217 (17), 129 (32), 117 (17); IR (neat): $\tilde{\nu}$=2957, 2930, 1709, 765, 700 cm^{-1}; R_f=0.58 (hexane/EtOAc 5:1). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.25; H, 9.05.

4.7.10. (*E*)-Isopropyl 3-cyclohexyl-2-methylprop-2-enoate (2j). Yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.57 (d, J=9.6 Hz, 1H), 5.06 (apparent quint., J=6.3 Hz, 1H), 1.84 (s, 3H), 1.68–1.27 (m, 11H), 1.28 (d, J=6.3 Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 168.1 (C), 146.8 (CH), 136.4 (C), 67.5 (CH), 37.7 (CH), 31.9 (2×CH_2), 25.8 (2×CH_2), 25.6 (CH_2), 21.8 (2×CH_3), 12.3 (CH_3); MS (70 eV, EI) *m/z* (%) 210 $[M]^+$ (9), 168 (100), 151 (48), 82 (61), 43 (27); R_f=0.50 (hexane/EtOAc 5:1). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.33; H, 10.41.

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