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Preparation of (*Z*)-α-chloro-α,β-unsaturated ketones with total or high diastereoselectivity

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Abstract—(*Z*)-α-Chloroenones are obtained by reaction of α-chloro-β-hydroxyketones with acetic anhydride, pyridine and 4-dimethylaminopyridine with total or high diastereoselectivity and in high yield. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

α-Chloroenones are important intermediates in organic synthesis[1] and the development of effective general methods for the preparation of these compounds is of significant value. The obtention of α-chloroenones is generally achieved by C–C double bond formation with the Wittig reaction,[2] by elimination reactions from α,β-dihaloketones,[3] α,α-dihaloketones,[4] or α-halo-β-hydroxyketones,[5] and by halogenation of α,β-unsaturated ketones.[6]

However, most of these preparations are essentially restricted to the obtention of cyclic α-chloroenones, and in some cases among the scarce preparations published of non-cyclic α-chloroenones, a mixture of different compounds or diastereoisomers are isolated, whilst in others the α-chloroenones are obtained in poor yields. Moreover, few of these methods are inexpensive, convenient, and use commercial reagents.

In connection with our interest in the synthesis of functionalized alkenes, in this communication, we describe a general preparation of (*Z*)-α-chloro-α,β-unsaturated ketones from the easily available, α-chloro-β-hydroxyketones, by treatment with the inexpensive reagents, acetic anhydride, pyridine and 4-dimethylaminopyridine (DMAP). Previously, a similar preparation had been described by Narita and co-workers.[5] However, this last methodology uses more expensive reagents (methanesulfonyl chloride, triethylamine and 1,8-diazabicyclo[5.4.0]undec-7-ene in CH_2Cl_2); the (*Z*)-α-chloroenones are obtained in good yield, but unpurified, in some cases, with the corresponding enones and no synthesis of aromatic (*Z*)-α-chloroenones are described. This led us to look for a more convenient preparation of these compounds.

2. Results and discussion

The reaction of several α-chloro-β-hydroxyalkanones **1** with acetic anhydride and pyridine in the presence of a catalytic amount of DMAP at 0°C afforded, after hydrolysis, the corresponding (*Z*)-α-chloroenones **2** with total or very high diastereoselectivity and in high yield (Scheme 1 and Table 1). The three reagents (acetic anhydride, pyridine, and DMAP) used in this process are necessary to carry out the transformation, and the elimination reaction does not take place in the absence of any one of them. So, when compounds **1** were treated with Ac_2O/Py or with Ac_2O/DMAP the *O*-acetyl ketone **7** was isolated instead of compound **2**.

The aromatic compounds **1a–c** were easily obtained by reaction of the corresponding potassium enolate of the

Table 1. Synthesis of (*Z*)-α-chloroenones

Entry	Product	R^1	R^2	Reaction time (h)	Yield (%)[a]	de[b]
1	**2a**[c]	Ph	C_4H_9	4	90	76
2	**2a**	Ph	C_4H_9	4	84	>98
3	**2b**	Ph	C_7H_{15}	4	88	>98
4	**2c**	Ph	Cyclohexyl	18	87	89
5	**2d**	Ph	$CH_3CH(Ph)$	18	70	>98
6	**2e**	Ph	Ph	2	80	>98
7	**2f**	Ph	*p*-Cl–C_6H_4	2	82	>98
8	**2g**	C_4H_9	C_4H_9	32	70	>98
9	**2h**	C_4H_9	Ph	18	78	>98

[a] Isolated yield after column chromatography based on the starting carbonyl compound **1**.
[b] de determined by 300 MHz ^{1}H NMR spectroscopy and GC–MS analysis on the crude product.
[c] This reaction was carried out at room temperature instead of at 0°C.

Keywords: α-chloroenones; elimination reactions; diastereoselection.

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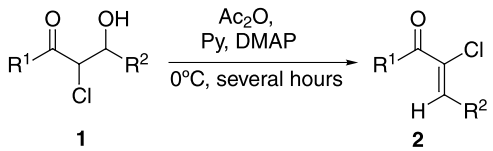


Scheme 1.

2-chloroacetophenone **3** [generated by treatment of 2-chloroacetophenone **3** with potassium hexamethyldisilazide (KMDS) at −78°C] with different aldehydes, at temperature ranging from −78 to 25°C. The obtained epoxyketones **4** were treated with chlorotrimethylsilane (TMSCl) and dimethylsulphoxide (DMSO), yielding the corresponding 2-chloro-3-hydroxyketones **1a–c**[7] (Scheme 2). Compounds **1d–f** were obtained by reaction of the lithium or potassium enolate of the 2-chloroacetophenone **3** (generated from 2-chloroacetophenone **3** and LDA or KHMDS at −85°C) with the corresponding aldehyde and further hydrolysis at −85°C (Scheme 2). Compounds **1g** and **h** were prepared by reaction of the ester **5** with bromochloromethyllithium obtaining the 1-bromo-1-chlorohexan-2-one **6**, which was treated with the corresponding aldehyde in the presence of Zn/CuBr/Et_2AlCl (Scheme 3).[8] It is noteworthy that although the starting compounds **1** were used as mixtures of diastereoisomers (roughly 1:1), the corresponding α-chloroenones **2** were obtained with total stereoselectivity.

By using this methodology, it is possible to afford aromatic and aliphatic chloroenones, in which the double bond C–C can be connected to aliphatic (linear, branched or cyclic) or aromatic groups.

The diastereoisomeric excess in the formation of the C–C double bond was determined on the crude reaction products by ^{1}H NMR spectroscopy (300 MHz) and GC–MS. The *Z* stereochemistry in the C–C double bond of chloroenones **2** was assigned by NOESY experiments (compounds **2b–d** and **2h**). In these experiments, a positive NOE was observed between the olefinic proton and the R^1 substituent (Ph in **2b–d** and Pr^nCH_2 in **2h**) showing a *cis* relationship between the chloro atom and the R^2.

The transformation of **1** into **2** may be explained taking into account that reaction of **1** (Scheme 4) with acetic anhydride, in the presence of DMAP, affords the *O*-acetyl ketone **7**, to facilitate the elimination reaction. Compound **7** were isolated and characterized by ^{13}C NMR after treatment of **1** with Ac_2O/Py or Ac_2O/DMAP. The reaction with pyridine promotes the elimination reaction affording the α-chloroenone **2**. The stereochemistry of **2** can be explained by assuming that the diastereoisomer **7A** suffers an *anti*-elimination through the transition state (its Newman projection is shown in Scheme 4) in which Cl and R^2 show a *cis* relationship and, consequently, an *anti*-elimination from **7A** affords (*Z*)-α-chloro-α,β-unsaturated ketones. The other diastereoisomer **7B** cannot suffer an *anti*-elimination due to the corresponding transition state cannot be reached by steric hindrance between R^1CO and R^2 groups, and undergoes an enolization reaction, leading by protonation, to the diastereoisomer **7A**, which by an elimination affords the α-chloroenone **2**.

To support this mechanism, the geometry of the conformations (shown in Scheme 4) of the diastereoisomers **7A** and **7B** (R^1=Ph, R^2=C_4H_9) were optimized by using the AM1 semiempirical method.[9] The conformation of diastereoisomer **7A** is predicted to be 2.7 kcal/mol more stable than diastereoisomer **7B**. According to this result, it can be expected that the *anti*-elimination of the acetyl group will take place, via the conformation of diastereoisomer **7A**, thus producing only the *Z* alkene, in good agreement with the experimental evidence. The steric interaction between the phenyl ring and the butyl group seems to be the responsible of the destabilization of the conformation of **7B**.

3. Conclusion

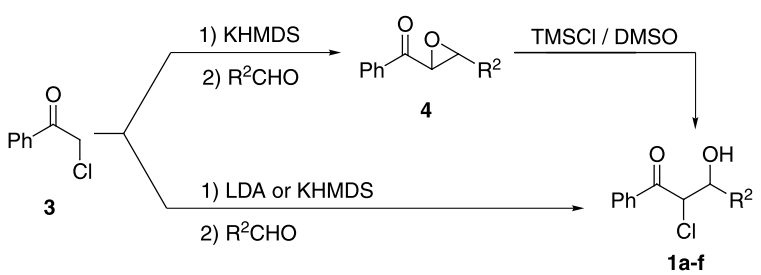
In conclusion, we have described a simple, easy, and convenient preparation of (*Z*)-α-chloroenones by using inexpensive commercial reagents.

4. Experimental

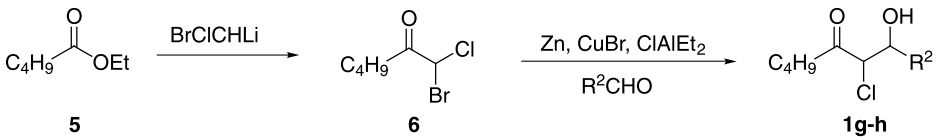
4.1. General

All reagents were purchased from Aldrich or Merck 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) and by cerium molybdate developer.

^{1}H NMR and ^{13}C NMR spectra were recorded on a BRUKER AC-200, AC-300 and on a DPX-300 spectrometers. Chemical shifts are given in δ (ppm) relative to TMS as internal standard in the case of ^{1}H NMR spectra and relative to $CDCl_3$ in the case of ^{13}C NMR spectra.



Scheme 2.



Scheme 3.

IR spectra were run in NaCl cells on a UNICAM MATTSON 3000 FTIR spectrometer. Mass spectra were recorded on a MD 800 GC 8000 series FISONS Instruments spectrometer by using EI 70 eV. Only the most important IR absorptions (in cm^{-1}) and the most important peaks in MS are given.

4.2. General method for the synthesis of α-chloro-β-hydroxyketones 1a–c

To a stirred solution of 2-chloroacetophenone **3** (5 mmol) in dry THF (25 mL), a solution of potassium hexamethyldisilazide 0.1 M in toluene (5.5 mmol) was added dropwise, at −78°C. The mixture was stirred at this temperature for 10 min and then a solution of aldehyde (7.5 mmol) in dry THF (5 mL) was added dropwise. The mixture was stirred overnight allowing the temperature to rise to room temperature. The reaction was quenched with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 and concentrated under reduced pressure, yielding pure α,β-epoxyketones **4**.

Crude epoxyketones **4** (5 mmol) were dissolved in dry acetonitrile (5 mL) and then trimethylchlorosilane (15 mmol) and dimethyl sulphoxide (15 mmol) were added slowly. The reaction was kept at room temperature by external cooling. After 30 min, the mixture was poured into water and extracted with diethyl ether. The organic layer was dried and then evaporated. The residue was purified by flash column chromatography on silica gel (eluent: hexane–ethyl acetate=10:1).

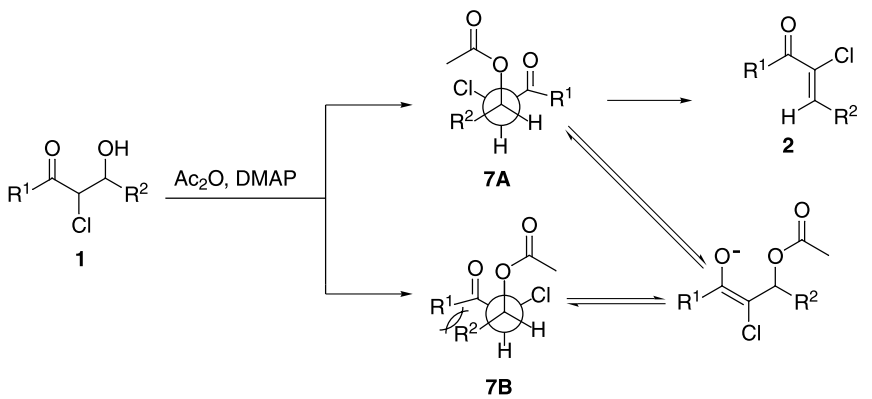
4.2.1. 2-Chloro-3-hydroxy-1-phenylheptan-1-one (1a). Yield: 92% (obtained as the *anti* diastereoisomer).[10] ^1H NMR (300 MHz, $CDCl_3$): δ=8.1–7.2 (m, 5H), 4.93 (d, 1H, *J*=7.96 Hz), 4.21 (dt, 1H, *J*=7.96, 2.32 Hz), 3.75–3.30 (br s, 1H), 1.92–1.86 (m, 6H), 0.92 (t, 3H, *J*=6.92 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.3 (C), 134.5 (C), 133.9 (CH), 128.9 (CH), 128.6 (CH), 71.6 (CH), 57.6 (CH), 32.3 (CH_2), 27.2 (CH_2), 22.3 (CH_2), 13.8 (CH_3). IR ν_{max}=3476, 3086, 2956, 2870, 1688, 1596, 1448 cm^{-1}. MS *m/z* 205 $[M-Cl]^+$ (3), 154 (12), 123 (25), 105 (100), 78 (14), 77 (44), 51 (12), 41 (19). R_f=0.36 (hexane–ethyl acetate=5:1).

4.2.2. 2-Chloro-3-hydroxy-1-phenyldecan-1-one (1b). Yield: 85% (obtained as the *anti* diastereoisomer).[10] ^1H NMR (300 MHz, $CDCl_3$): δ=8.01–7.45 (m, 5H), 4.94 (d, 1H, *J*=7.94 Hz), 4.22 (dt, 1H, *J*=7.94, 2.10 Hz), 4.10–3.50 (br s, 1H), 2.02–1.83 (m, 12H), 0.89–0.85 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=194.2 (C), 134.5 (C), 133.8 (CH), 128.8 (CH), 128.6 (CH), 71.5 (CH), 57.6 (CH), 32.5 (CH_2), 31.6 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 25.0 (CH_2), 22.4 (CH_2), 13.9 (CH_3). IR ν_{max}=3387, 3063, 2951, 2923, 2855, 1689, 1596, 1581, 1464, 1449 cm^{-1}. MS *m/z* 247 $[M-Cl]^+$ (5), 156 (5), 154 (16), 123 (20), 106 (8), 105 (100), 78 (13), 77 (38), 43 (21), 41 (22). R_f=0.45 (hexane–ethyl acetate=5:1).

4.2.3. 2-Chloro-3-cyclohexyl-3-hydroxy-1-phenylpropan-1-one (1c). Yield: 93% (obtained as the *anti* diastereoisomer).[10] ^1H NMR (300 MHz, $CDCl_3$): δ=8.00–7.26 (m, 5H), 5.08 (d, 1H, *J*=8.46 Hz), 4.07 (ddd, 1H, *J*=8.46, 6.16, 4.6 Hz), 2.96 (d, 1H, *J*=6.16 Hz), 2.18–1.22 (m, 11H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=194.6 (C), 134.7 (C), 133.8 (CH), 128.9 (CH), 127.8 (CH), 75.1 (CH), 53.8 (CH), 38.5 (CH), 29.9 (CH_2), 28.9 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 25.2 (CH_2). IR ν_{max}=3507, 3058, 2923, 2852, 1683, 1596, 1580, 1448, 1392, 1265, 1208, 1071 cm^{-1}. MS *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). R_f=0.47 (hexane–ethyl acetate=5:1).

4.3. General method for the synthesis of hydroxyketone 1d

To a stirred solution of 2-chloroacetophenone **3** (5 mmol) in dry THF (25 mL), a solution of potassium hexamethyldisilazide 0.1 M in toluene (5.5 mmol) was added dropwise, at −85°C. The mixture was stirred at this temperature for 10 min and then a solution of 2-phenylpropanal (7.5 mmol)



Scheme 4.

in dry THF (5 mL) was added dropwise. The mixture was stirred 15 min at the same temperature. The reaction was quenched with saturated aqueous NH_4Cl and usual workup yielded crude hydroxyketone **1d**, which were purified by flash column chromatography (eluent: hexane–ethyl acetate=10:1).

4.3.1. 2-Chloro-3-hydroxy-1,4-diphenylpentan-1-one (1d). Yield: 75% (obtained as one diastereoisomer). ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.58–7.15 (m, 10H), 4.90 (d, 1H, J=1.54 Hz), 4.23 (dd, 1H, J=1.54 Hz, J=9.50 Hz), 3.30–3.25 (br s, 1H), 3.16 (dc, 1H, J=9.50, 6.92 Hz), 1.48 (d, 3H, J=6.92 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.8 (C), 142.5 (C), 133.6 (CH), 133.5 (C), 128.6 (CH), 128.4 (CH), 128.3 (CH), 127.3 (CH), 126.9 (CH), 75.3 (CH), 60.4 (CH), 42.9 (CH), 17.6 (CH_3). IR ν_{max}=3517, 3060, 2968, 2932, 2875, 1688, 1596, 1580, 1450, 1224, 1013 cm^{-1}. MS m/z 289 [M]$^+$ (10), 235 (7), 187 (12), 186 (100), 155 (7), 102 (27). R_f=0.33 (hexane–ethyl acetate=5:1).

4.4. General method for the synthesis of α-chloro-β-hydroxyketones 1e and 1f

2-Chloroacetophenone **3** (4.5 mmol) was dissolved in 2 mL of dry THF and added over a solution of lithium diisopropylamide in THF [prepared from MeLi (5 mmol of a solution 1.5 M in diethyl ether) and diisopropylamine (5 mmol) in THF (25 mL) at 0°C] at −90°C. After stirring for 10 min, the corresponding aromatic aldehyde (6.75 mmol) in THF (4 mL) was added dropwise at the same temperature and the reaction mixture was stirred for 15 min at the same temperature. Then it was quenched with saturated aqueous NH_4Cl and usual workup yielded crude hydroxyketones **1e** and **1f**, which were purified by flash column chromatography (eluent: hexane–ethyl acetate=10:1).

4.4.1. 2-Chloro-3-hydroxy-1,3-diphenylpropan-1-one (1e). Yield: 80% (obtained as a mixture 3:2 of *syn*/*anti* diastereoisomers).[10] ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.05–7.28 (m, 20H), 5.37 (d, 1H, J=5.78 Hz), 5.31 (d, 1H, J=5.78 Hz), 5.30 (d, 1H, J=8.55 Hz), 5.20 (d, 1H, J=8.55 Hz), 3.80–3.60 (br s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=194.3 (C), 194.0 (C), 139.1 (C), 138.5 (C), 134.5 (C), 134.0 (CH), 128.9 (CH), 128.7 (CH), 128.6 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.1 (CH), 126.7 (CH), 74.5 (CH), 73.2 (CH), 61.3 (CH), 57.4 (CH). IR ν_{max}=3504, 3087, 3032, 1964, 1903, 1813, 1695, 1595, 1580, 1453, 1307, 1062 cm^{-1}. R_f=0.34 (hexane–ethyl acetate=5:1).

4.4.2. 2-Chloro-3-(4-chlorophenyl)-3-hydroxy-1-phenylpropan-1-one (1f). Yield: 76% (obtained as a mixture 3:5 of *syn*/*anti* diastereoisomers).[10] ^{1}H NMR (200 MHz, $CDCl_3$): δ=8.04–7.27 (m, 18H), 5.36 (d, 1H, J=5.14 Hz), 5.26 (d, 1H, J=8.44 Hz), 5.24 (d, 1H, J=5.14 Hz), 5.12 (d, 1H, J=8.44 Hz), 3.94–3.92 (br s, 1H), 3.90–3.75 (br s, <1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=194.2 (C), 194.1 (C), 137.6 (C), 137.1 (C), 134.3 (CH), 134.2 (CH), 134.1 (C), 133.9 (C), 129.0 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 73.7 (CH), 72.5 (CH), 60.8 (CH), 57.2 (CH). IR ν_{max}=3057, 3081, 3062, 3037, 2936, 2903, 1685, 1596, 1490, 1449, 1400, 1372, 1316, 1227, 1086, 1013 cm^{-1}. R_f=0.33 (hexane–ethyl acetate=3:1).

4.5. General method for the synthesis of α-chloro-β-hydroxyketones 1g–h

To a solution of lithium diisopropylamide in dry THF [prepared from MeLi (20 mmol of a solution 1.5 M in diethyl ether) and diisopropylamine (20 mmol) in THF (40 mL) at 0°C] was added very slowly chlorobromomethane (20 mmol) in THF (5 mL) at −95°C. After stirring for 15 min, a solution of ethyl pentanoate **5** (10 mmol) in THF (5 mL) was added dropwise to the solution of chlorobromomethyllithium, and the resulting mixture was stirred for 2.5 h at −95 to −60°C. The reaction was quenched with HCl 1 M, extracted with ether, washed with brine, dried (Na_2SO_4), and concentrated. The residual oil was purified by silica gel column chromatography (eluent: ether–hexane=1:40) if it was necessary, but in general the obtained 1-bromo-1-chlorohexan-2-one **6** could be used without further purification.

A solution of diethylaluminum chloride (10 mmol) 1.0 M in hexane was added to a slurry of zinc dust (10 mmol) and a catalytic amount of copper (I) bromide (0.93 mmol) in THF (40 mL) with stirring at 20°C over 0.5 h. The resulting mixture was cooled to −5°C, and a solution of the 1-bromo-1-chlorohexan-2-one (10 mmol) and the corresponding aldehyde (10 mmol) was added slowly over 20 min at −5°C. After 2 h at the same temperature, the reaction was quenched with saturated aqueous $NaHCO_3$, filtered over celite and extracted with diethyl ether. The ether extracts were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The obtained oil was purified by flash column chromatography on silica gel (eluent: hexane–ethyl acetate=10:1).

4.5.1. 1-Bromo-1-chlorohexan-2-one. Yield: 92%. ^{1}H NMR (200 MHz, $CDCl_3$): δ=5.87 (s, 1H), 2.85 (t, 2H, J=7.30 Hz), 1.71–1.57 (m, 2H), 1.44–1.57 (m, 2H), 0.87 (t, 3H, J=6.92 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ=197.1 (C), 57.0 (CH), 34.6 (CH_2), 25.9 (CH_2), 21.9 (CH_2), 13.6 (CH_3).

4.5.2. 6-Chloro-7-hydoxyundecan-5-one (1g). Yield: 75% (obtained as a mixture 2:1 of *syn*/*anti* diastereoisomers).[10] ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.25 (d, 1H, J=3.42 Hz), 4.12–4.08 (m, 3H), 2.75–2.66 (m, 4H), 1.65–1.27 (m, 20H), 0.93 (t, 12H, J=7.17 Hz). ^{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 (CH_2), 32.6 (CH_2), 27.5 (CH_2), 27.2 (CH_2), 25.3 (CH_2), 22.3 (CH_2), 22.0 (CH_2), 13.8 (CH_3), 13.7 (CH_3). IR ν_{max}=3427, 2958, 2932, 2872, 1711, 1466, 1379 cm^{-1}. MS m/z 185 [M−Cl]$^+$ (7), 134 (9), 118 (10), 103 (100), 92 (36), 85 (90), 69 (23), 57 (97), 56 (34), 43 (27), 41 (77). R_f=0.23 (hexane–ethyl acetate=10:1).

4.5.3. 2-Chloro-1-hydroxy-1-phenylheptan-3-one (1h). Yield: 61% (obtained as a mixture 1:1 of *syn*/*anti* diastereoisomers).[10] ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.4–7.3 (m, 10H), 5.16 (d, 1H, J=5.38 Hz), 5.01 (d, 1H, J=8.22 Hz), 4.44 (d, 1H, J=5.38 Hz), 4.35 (d, 1H, J=8.22 Hz), 3.60–3.35 (br s, 2H), 2.67–2.30 (m, 4H),

1.66–2.30 (m, 8H), 0.91 (t, 3H, J=6.92 Hz), 0.86 (t, 3H, J=7.18 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ=205.5 (C), 205.2 (C), 139.0 (C), 138.7 (C), 128.4 (CH), 128.3 (CH), 128.2 (CH), 126.8 (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 ν_{max}=3460, 3088, 3064, 3033, 2957, 2872, 1714, 1604, 1495, 1454, 1380, 1267, 1050 cm^{-1}. MS m/z 205 [M−Cl]$^+$ (14), 140 (33), 138 (61), 134 (20), 107 (100), 105 (32), 92 (47), 91 (32), 85 (52), 79 (72), 77 (80), 57 (90), 51 (36), 41 (89). R_f=0.30 (hexane–ethyl acetate=5:1).

4.6. General method for the preparation of (*Z*)-α-chloro-α,β-unsaturated ketones

To the corresponding α-chloro-β-hydroxyketone **1** (0.4 mmol) were added pyridine (5 mL), acetic anhydride (5 mL) and 4-dimethylaminopyridine (5 mg) at 0°C. After the time indicated in Table 1, the reaction mixture was poured into a mixture of water–ice, and then extracted with diethyl ether. The organic layer was successively washed with HCl (4×5 mL) and with H_2O (4×20 mL), was dried over anhydrous sodium sulphate and the solvents were distilled to afford the corresponding α-chloroenones **2** crude, which were purified by column flash chromatography over silica gel (eluent: hexane–ethyl acetate=10:1) to provide pure compounds **2**.

4.6.1. (*Z*)-2-Chloro-1-phenylhept-2-en-1-one[11] (2a). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.69–7.46 (m, 5H), 6.66 (t, 1H, J=7.11 Hz), 2.47 (dt, 2H, J=7.11, 7.11 Hz), 1.50–1.32 (m, 4H), 0.92 (t, 3H, J=7.26 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ=190.1 (C), 145.4 (CH), 136.8 (C), 133.0 (C), 132.2 (CH), 129.2 (CH), 128.2 (CH), 29.7 (CH_2), 29.4 (CH_2), 22.3 (CH_2), 13.6 (CH_3). IR ν_{max}=3062, 3028, 2959, 2929, 2861, 1668, 1615, 1598, 1447, 1379, 1317, 1266 cm^{-1}. MS m/z 222 [M]$^+$ (5), 179 (12), 157 (9), 129 (15), 115 (29), 105 (100), 77 (89), 51 (33), 41 (21). R_f=0.40 (hexane–ethyl acetate=10:1).

4.6.2. (*Z*)-2-Chloro-1-phenyldec-2-en-1-one (2b). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.52–7.37 (m, 5H), 6.66 (t, 1H, J=7.26 Hz), 2.46 (dt, 2H, J=7.26, 7.38 Hz), 1.49–1.28 (m, 10H), 0.89 (t, 3H, J=6.66 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ=190.2 (C), 145.6 (CH), 136.8 (C), 133.0 (C), 132.2 (CH), 129.2 (CH), 128.2 (CH), 31.5 (CH_2), 29.8 (CH_2), 29.2 (CH_2), 28.8 (CH_2), 27.6 (CH_2), 22.5 (CH_2), 13.9 (CH_3). IR ν_{max}=3061, 3027, 2954, 2926, 2856, 1768, 1744, 1667, 1613, 1447, 1370, 1266, 1024 cm^{-1}. MS m/z 264 [M]$^+$ (<1%), 167 (11), 145 (11), 115 (21), 105 (100), 77 (72), 55 (9), 51 (16), 43 (26), 41 (29). Anal. calcd for $C_{16}H_{21}ClO$: C, 72.57; H, 7.99. Found: C, 72.60; H, 7.91. R_f=0.47 (hexane–ethyl acetate=10:1).

4.6.3. (*Z*)-2-Chloro-3-cyclohexyl-1-phenylpropenone (2c). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.67–7.41 (m, 5H), 6.50 (d, 1H, J=9.22 Hz), 2.87–2.68 (m, 1H), 1.84–1.34 (m, 5H), 1.29–1.13 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=190.4 (C), 149.9 (CH), 136.8 (C), 132.2 (CH), 130.9 (C), 129.3 (CH), 128.2 (CH), 38.9 (CH), 30.9 (CH_2), 25.6 (CH_2), 25.2 (CH_2). IR ν_{max}=3060, 3023, 2974, 2875, 2840, 1664, 1615, 1578, 1446, 1317, 1261, 1222 cm^{-1}. MS m/z 248 [M]$^+$ (100), 213 (37), 191 (25), 183 (27), 167 (34), 105 (74), 77 (36), 43 (77). Anal. calcd for $C_{15}H_{17}ClO$: C, 72.43; H, 6.89. Found: C, 72.32; H, 6.80. R_f=0.40 (hexane–ethyl acetate=10:1).

4.6.4. (*Z*)-2-Chloro-1,4-diphenylpent-2-en-1-one (2d). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.68–7.25 (m, 10H), 6.77 (d, 1H, J=9.66 Hz), 4.28 (dc, 1H, J=9.66, 7.11 Hz), 1.50 (d, 3H, J=7.11 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ=190.2 (C), 148.4 (CH), 142.5 (C), 136.5 (C), 132.5 (CH), 131.3 (C), 129.4 (CH), 128.7 (CH), 128.3 (CH), 126.9 (CH), 39.9 (CH), 19.9 (CH_3). IR ν_{max}=3084, 3060, 3027, 2970, 2929, 2872, 1755, 1666, 1598, 1493, 1447, 1241 cm^{-1}. MS m/z 270 [M]$^+$ (6), 234 (4), 191, (8), 129 (9), 115 (10), 105 (100), 77 (72), 51 (21). Anal. calcd for $C_{17}H_{15}ClO$: C, 75.41; H, 5.58. Found: C, 75.29; H, 5.51. R_f=0.37 (hexane–ethyl acetate=10:1).

4.6.5. (*Z*)-2-Chloro-1,3-diphenylpropen-1-one[6] (2e). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.86–7.17 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=191.1 (C), 139.7 (CH), 136.6 (C), 132.6 (C), 132.4 (CH), 130.5 (CH), 130.3 (CH), 130.2 (C), 129.3 (CH), 128.4 (CH), 128.3 (CH). IR ν_{max}=3059, 3026, 1964, 1908, 1814, 1771, 1730, 1667, 1600, 1491, 1447, 1251 cm^{-1}. MS m/z 242 [M]$^+$ (11), 241 (6), 207 (15), 105 (72), 77 (100), 51 (48). R_f=0.33 (hexane–ethyl acetate=10:1).

4.6.6. (*Z*)-2-Chloro-3-(4-chlorophenyl)-1-phenylpropen-1-one[12] (2f). ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.81–7.38 (m, 10H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=190.8 (C), 138.0 (CH), 136.4 (C), 136.2 (C), 132.5 (CH), 131.7 (CH), 131.1 (C), 130.7 (C), 129.4 (CH), 128.7 (CH), 128.4 (CH). IR ν_{max}=3062, 3028, 1661, 1605, 1563, 1490, 1447, 1404, 1247, 1204, 1180, 1088, 1013 cm^{-1}. MS m/z 276 [M]$^+$ (27), 241 (63), 212 (6), 176 (6), 163 (7), 136 (15), 105 (100), 77 (69), 51 (19). R_f=0.33 (hexane–ethyl acetate=10:1).

4.6.7. (*Z*)-6-Chloroundec-6-en-5-one (2g). ^{1}H NMR (200 MHz, $CDCl_3$): δ=6.94 (t, 1H, J=7.18 Hz), 2.73 (t, 2H, J=7.30 Hz), 2.38 (dt, 2H, J=7.18, 7.18 Hz), 1.64–1.26 (m, 8H), 0.95–0.88 (m, 6H).^{13}C NMR (50 MHz, $CDCl_3$): δ=194.5 (C), 140.6 (CH), 133.4 (C), 38.1 (CH_2), 29.8 (CH_2), 29.1 (CH_2), 26.3 (CH_2), 22.3 (CH_2), 22.2 (CH_2), 13.7 (CH_3), 13.6 (CH_3). IR ν_{max}=2960, 2872, 1768, 1744, 1696, 1617, 1465, 1403, 1379, 1236, 1160, 1094, 1021 cm^{-1}. MS m/z 202 [M]$^+$ (<1%), 173 (14), 160 (66), 145 (100), 131 (28), 125 (18), 118 (17), 104 (74), 89 (43), 85 (29), 81 (41), 57 (69), 53 (32). Anal. calcd for $C_{11}H_{19}ClO$: C, 65.17; H, 9.45. Found: C, 65.01; H, 9.51. R_f=0.33 (hexane–ethyl acetate=20:1).

4.6.8. (*Z*)-2-Chloro-1-phenylhept-1-en-3-one (2h). ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.88–7.81 (m, 2H), 7.77 (s, 1H), 7.50–7.37 (m, 3H), 2.89 (t, 2H, J=7.30 Hz), 1.77–1.62 (m, 2H), 1.50–1.28 (m, 2H), 0.97 (t, 3H, J=7.17 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ=195.6 (C), 134.6 (CH), 132.8 (C), 130.7 (CH), 130.1 (CH), 130.0 (C), 128.4 (CH), 38.3 (CH_2), 26.3 (CH_2), 22.2 (CH_2), 13.8 (CH_3). IR ν_{max}=3056, 2958, 2932, 2872, 1688, 1597, 1574, 1491, 1400, 1265, 1142, 1008 cm^{-1}. MS m/z 222 [M]$^+$ (28), 180 (54), 165 (51), 145 (100), 137 (40), 102 (57), 57 (26). Anal. calcd for $C_{13}H_{15}ClO$: C, 70.11; H, 6.79. Found: C, 70.22; H, 6.69. R_f=0.4 (hexane–ethyl acetate=20:1).

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