Synthesis of β-lactones. Part 7.[1] α-Chloro- and α,α-dichloro-β-lactones by aldolization of carbonyl compounds with lithium ester enolates derived from chlorinated phenyl alkanoates: an unusual course of the Darzens reaction

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α-Chlorinated β-lactones are obtained in a one-step reaction at a temperature < −78 °C by condensation of ketones or aldehydes with ester enolates derived from phenyl α-chloroalkanoates or α,α-dichloroethanoate. The intermediate *O*-lithiated phenyl α-chloro-β-hydroxyalkanoates eliminate lithium phenoxide instead of lithium chloride, thus causing the Darzens reaction to take an unusual course. Irrespective of the low diastereoselectivity of this process, it is in many cases superior to other known processes for the synthesis of α-chlorinated β-lactones.

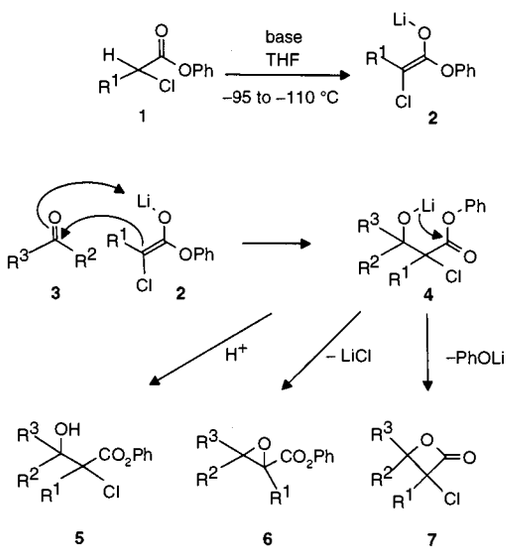
Introduction

The formation of *O*-metallated alkyl 2-halogeno-3-hydroxyalkanoates by addition of aldehydes or ketones to enolates derived from alkyl 2-halogenoalkanoates is known as the first step of the Darzens reaction.[2] Subsequent elimination of metal halide leads in a second step to alkyl glycidates (alkyl 2,3-epoxyalkanoates). This reaction has been used during the last 100 years for the synthesis of a large variety of glycidic esters[3] as well as for the preparation of aldehydes[4] and ketones[5] by hydrolysis and decarboxylation of the glycidates. In connection with a series of β-lactone syntheses,[1,6] especially with those involving the addition of indium or lithium phenyl ester enolates[7,8] to ketones or aldehydes, elaborated in our laboratory during the last 5 years, we were interested in the addition of lithium enolates derived from phenyl esters of α-chlorinated carboxylic acids to ketones and aldehydes. A survey of the literature[3] revealed that Darzens reactions have generally been performed with alkyl esters. To the best of our knowledge, however, phenyl esters have never been used in this reaction. We therefore started an investigation with the aim of clarifying whether the addition of lithium ester enolates of phenyl α-chloroalkanoates to carbonyl compounds affords glycidic esters according to Darzens' route, or α-chloro-β-lactones according to our procedures.[7–9]

Results and discussion

For this purpose the phenyl esters of 2-chloropropanoic acid **1A**, 2-chlorobutanoic acid **1B** and 2,2-dichloroethanoic acid **1C** were converted into the corresponding enolates **2** and treated with the ketones **3a–f** or the aldehydes **3g–i**. The first experiment, in which **1A** was transformed with lithium *N*-cyclohexyl-*N*-isopropylamide (LiICA) at −78 °C into **2A** and condensed with cyclohexanone **3a**, afforded the α-chloro-β-lactone **7Aa** in high yield (Table 1, entry 1). Neither the α-chloro-β-hydroxy ester **5Aa** nor the glycidic ester **6Aa** could be detected in the reaction mixture. The success of this reaction is based on the fact that the phenoxide group in the intermediate **4Aa** is a better leaving group than the chloride. Lithium phenoxide is therefore eliminated instead of lithium chloride.

The reaction of the phenyl ester enolate **2A** with the ketones **3b–f** afforded the corresponding β-lactones **7Ab–Af** in yields of >70% (entries 2–6) except **7Ad**, which was obtained only in a yield of 43% (entry 4). The yields of α,β-dialkyl-α-chloro-β-lactones from **2A** and the aldehydes **3g–i** were generally lower (entries 7–9). Best results were obtained with the non-enolizable aldehyde **3g** (entry 7).



1, 2	R^1
A	Me
B	Et
C	Cl

3	R^2	R^3
a	$-(CH_2)_5-$	
b	$-(CH_2)_4-$	
c	Et	Et
d	Me	Me
e	Et	Me

3	R^2	R^3
f	Ph	Me
g	Bu^t	H
h	c-C_6H_{11}	H
i	$Ph(CH_2)_2$	H

Scheme 1

The tendency for α,β,β-trialkyl-α-chloro-β-lactones from ketones to be obtained in higher yields than α,β-dialkyl-α-chloro-β-lactones from aldehydes was observed also for the formation of the β-lactones **7Ba–Bi** from phenyl 2-chlorobutanoate **1B** (entries 10–18).

The greater suitability of ketones for this β-lactone synthesis became even more evident, when phenyl 2,2-dichloroethanoate **1C** was treated with the carbonyl compounds **3a–i**. The ketones **3a–e** provided the β,β-dialkyl-α,α-dichloro-β-lactones **7Ca–Ce** in yields of 36–95% (entries 19–23), whereas cyclohexanecarbaldehyde **3h** and 3-phenylpropanal **3i**, and even acetophenone

Table 1 α-Chloro-β-lactones **7** prepared from the phenyl α-chloroalkanoates **1**

Entry	β-Lactone **7**	R^1	R^2	R^3	Base	Yield of **7** (%)
1	**7Aa**	Me	$-(CH_2)_5-$		LiICA	93
2	**7Ab**	Me	$-(CH_2)_4-$		LiICA	72
3	**7Ac**	Me	Et	Et	$LiN(SiMe_3)_2$	81
4	**7Ad**	Me	Me	Me	$LiN(SiMe_3)_2$	43
5	**7Ae**	Me	Et	Me	$LiN(SiMe_3)_2$	70
6	**7Af**	Me	Ph	Me	LiICA	83
7	**7Ag**	Me	Bu^t	H	$LiN(SiMe_3)_2$	64
8	**7Ah**	Me	c-C_6H_{11}	H	LiICA	37
9	**7Ai**	Me	$Ph(CH_2)_2$	H	$LiN(SiMe_3)_2$	53
10	**7Ba**	Et	$-(CH_2)_5-$		LiICA	83
11	**7Bb**	Et	$-(CH_2)_4-$		LiICA	80
12	**7Bc**	Et	Et	Et	LiICA	68
13	**7Bd**	Et	Me	Me	LiICA	72
14	**7Be**	Et	Et	Me	LiICA	73
15	**7Bf**	Et	Ph	Me	LiICA	78
16	**7Bg**	Et	Bu^t	H	LiICA	62
17	**7Bh**	Et	c-C_6H_{11}	H	LiICA	37
18	**7Bi**	Et	$Ph(CH_2)_2$	H	LiICA	40
19	**7Ca**	Cl	$-(CH_2)_5-$		$LiN(SiMe_3)_2$	95
20	**7Cb**	Cl	$-(CH_2)_4-$		$LiN(SiMe_3)_2$	54
21	**7Cc**	Cl	Et	Et	$LiN(SiMe_3)_2$	78
22	**7Cd**	Cl	Me	Me	$LiN(SiMe_3)_2$	36
23	**7Ce**	Cl	Et	Me	$LiN(SiMe_3)_2$	60
24	**7Cf**	Cl	Ph	Me	$LiN(SiMe_3)_2$	—
25	**7Cg**	Cl	Bu^t	H	$LiN(SiMe_3)_2$	37
26	**7Ch**	Cl	c-C_6H_{11}	H	$LiN(SiMe_3)_2$	—
27	**7Ci**	Cl	$Ph(CH_2)_2$	H	$LiN(SiMe_3)_2$	—

3f failed to form the corresponding β-lactones **7Ch**, **7Ci** and **7Cf** (entries 26, 27 and 24). Only the non-enolizable pivalaldehyde **3g** afforded the lactone **7Cg** in a yield of 37%.

There are two reasons for the superiority of ketones in this β-lactone synthesis. On the one hand, the geminal dialkyl effect favours the formation of higher substituted four-membered rings,[10] whilst on the other hand, ketones do not form 1,3-dioxan-4-ones in a competitive side-reaction.[11]

In many cases the amine used for the generation of the phenyl ester enolates **2** was crucial. The ester enolate **2C** provided the corresponding β-lactones **7C** only if the phenyl 2,2-dichloroethanoate **1C** was deprotonated with lithium hexamethyldisilazide [$LiN(SiMe_3)_2$]. Deprotonation with lithium diisopropylamide (LDA) or lithium *N*-cyclohexyl-*N*-isopropylamide (LiICA) proved to be unsuccessful. The phenyl 2-chloroalkanoates **1A** and **1B**, however, provided the β-lactones **7A** and **7B** after deprotonation with LiICA as well as with $LiN(SiMe_3)_2$. Nevertheless, LiICA was preferred for the preparation of β-lactones from **1B**, since this base afforded better yields especially in the cases of entries 15, 17 and 18. No systematic trend could be recognized for the preparation of β-lactones from **1A**. For **7Ac**, **7Ad** and **7Ah**, LiICA and $LiN(SiMe_3)_2$ gave comparable yields. In all other cases the base given in Table 1 was the superior one. It is known that the stability of an ester enolate depends on the base used for the deprotonation.[12] It could be shown that lithium ester enolates derived from ethyl and *tert*-butyl alkanoates by use of LiICA at −78 °C do not tend to self-condensation and are stable even at room temperature.[13] Lithium enolates derived from phenyl alkanoates or phenyl 2-chloroalkanoates seem to be more reactive and less stable. In order to get optimal yields of β-lactones it was therefore necessary to perform the reaction at a temperature of −78 °C or even lower. Ester enolates derived from phenyl 2,2-dichloroethanoate were shown to be still more unstable. For the formation of α,α-dichloro-β-lactones they had to be generated and then allowed to react at a temperature of −110 °C.

The β-lactones **7Ae**–**Ai** and **7Be**–**Bi**, obtained from phenyl α-chloroalkanoates and asymmetric ketones or aldehydes are mixtures of diastereoisomeric compounds. All β-lactones with (3*R**,4*R**)-configuration bear the alkyl group at C_α and the alkyl or aryl group of highest priority at C_β on the same side of the four-membered ring. They are therefore described in the discussion as *syn* compounds. Their diastereoisomers with a (3*R**,4*S**)-configuration exhibit these groups on different sides of the ring and are consequently designated as *anti* compounds.

The diastereoselectivity of the described β-lactone synthesis was low. In all relevant cases *syn* and *anti* compounds were formed in the order of 1:0.5 to 1:2. Only with acetophenone **3f** as the carbonyl compound were the *syn* diastereoisomers **7Af** and **7Bf** formed preferentially. A complete separation by flash chromatography was achieved for **7Af, 7Bf**, **7Bg** and **7Bi**. In all other cases the separation was incomplete or failed altogether (see Experimental section). The assignment of the *syn* or *anti* configuration was achieved on the basis of NOESY and NOE difference spectroscopy. β-Lactones obtained from aldehydes and the enolates **2A** or **2B** exhibit the signal for the C_β-proton of the *anti* diastereoisomer at 4.03–4.42 ppm and for that of the *syn* diastereoisomer at 4.32–4.65 ppm. In all cases, the signal for the *syn* diastereoisomer was shifted by 0.23–0.35 ppm to lower field. This is in agreement with earlier observations concerning the position of the signals of the C_β-proton in related unchlorinated diastereoisomers.[1,14]

Since the outlined β-lactone synthesis deviates from the normal course of the Darzens reaction only in the second step when lithium phenoxide is eliminated instead of lithium chloride, the low diastereoselectivity is in agreement with the normal course of the classical glycidate synthesis. For example, the reaction of acetophenone[15] or benzaldehyde[16] with ethyl 2-bromopropanoate affords the corresponding *syn* and *anti* ethyl glycidates also in a ratio of *ca.* 1:1.

The reaction of the lithium phenyl ester enolates **2** with carbonyl compounds opens a new route to α-chlorinated β-lactones. The α-monochlorinated compounds have been prepared in a two-step procedure by addition of carbonyl compounds to dilithiated α-chloroalkanoic acids and subsequent cyclization with benzenesulfonyl chloride in pyridine[17] or by cycloaddition of α-chloro ketenes and activated carbonyl compounds.[18,19] The α,α-dichloro-β-lactones have been available by addition of dichloroketene to carbonyl compounds,[20] if necessary in the presence of a Lewis acid,[18,21] or by addition of carbonyl compounds to dilithiated 2,2-dichloroethanoic acid

and subsequent cyclization with benzenesulfonyl chloride.[22] There seems to exist only one example in the literature for the formation of a β-lactone in the course of a Darzens reaction.[23] The reported yield, however, was only 10%.

Conclusion

The condensation of a carbonyl compound with a lithium ester enolate derived from an α-chlorinated phenyl alkanoate opens a new route to α-chloro- and α,α-dichloro-β-lactones. This one-step procedure supplements the existing methods for the preparation of this class of compounds and gives better yields in many cases. It should be emphasized that the simple exchange of an alkyl ester by a phenyl ester changes the classical glycidic ester synthesis of the Darzens reaction to an efficient one-step synthesis of α-chlorinated β-lactones.

Experimental

IR spectra were measured from films or solutions of solids in CCl_4 using a Specord 75 IR instrument (Carl Zeiss Jena). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively, with tetramethylsilane as internal standard using a Varian Gemini 300 instrument; coupling constants (*J*) are given in Hz. Flash chromatography was performed on silica gel 60 (0.04–0.063 mm, E. Merck). Mixtures of hexane and ethyl acetate were used as eluents. The phenyl 2-chloroalkanoates **1A**–**C** were prepared by heating the corresponding alkanoyl chlorides and phenol with a trace of H_2SO_4 in refluxing toluene following the literature.[24] The ketones and aldehydes **3** were purchased from Aldrich and Fluka and used without further purification.

General procedure for the preparation of the α-chloro-β-lactones 7A and 7B from the α-chloro phenyl esters 1A or 1B and the carbonyl compounds 3

A 1.35 M solution of butyllithium in hexane (4.4 cm^3, 6.0 mmol) was added by syringe at a temperature of 0 °C during 1 min to *N*-cyclohexyl-*N*-isopropylamine (1.10 cm^3, 6.6 mmol) or hexamethyldisilazane (1.37 cm^3, 6.6 mmol) in THF (20 cm^3). The mixture was allowed to warm up to ambient temperature within 15 min and thereafter cooled to −95 °C (liquid nitrogen–ethanol bath). Then one of the α-chloro phenyl esters **1A** or **1B** (6 mmol) dissolved in THF (5 cm^3) was pre-cooled with acetone–solid CO_2 to *ca.* −50 °C in a dropping funnel equipped with a cooling jacket. This solution was slowly added during a period of 30 min to the lithium amide. During the addition the temperature was kept at −90 to −100 °C. After the mixture had been stirred for an additional 20 min at this temperature, a pre-cooled solution of the carbonyl compound **3** (5 mmol) in THF (5 cm^3) was added to it during 20 min from the dropping funnel, the temperature being kept at −90 to −100 °C. The mixture was then allowed to warm to 0 °C during 2 h. After addition of diethyl ether (50 cm^3), 1 M aqueous NaOH (15 cm^3, 15 mmol) and water (50 cm^3) to the mixture, the organic phase was separated, washed with 1 M aqueous NaOH (2 × 7.5 cm^3) and brine (2 × 20 cm^3), dried (Na_2SO_4), filtered and evaporated under reduced pressure to afford a pale yellow oil. The corresponding α-chloro-β-lactone **7** was isolated from this by flash chromatography on silica gel with hexane–ethyl acetate (10:1 to 30:1) as eluent. The yields of isolated products are given in Table 1 (entries 1–18). According to this general procedure the following α-chloro-β-lactones **7A** and **7B** have been prepared.

(±)-3-Chloro-3-methyl-1-oxaspiro[3.5]nonan-2-one 7Aa.[17a] Colourless solid, mp 65–70 °C; ν_{max}(CCl_4)/cm^{-1} 1841 (C=O); δ_H 1.76 (3 H, s, 3-CH_3) and 1.57–1.80 [10 H, m, $(CH_2)_5$]; δ_C 20.5, 22.6, 22.7, 24.4, 32.0, 33.7, 72.8, 87.7 and 168.6 (Found: C, 57.4; H, 7.0; Cl, 18.7. $C_9H_{13}ClO_2$ requires C, 57.3; H, 6.95; Cl, 18.8%).

(±)-3-Chloro-3-methyl-1-oxaspiro[3.4]octan-2-one 7Ab.[17a] Colourless oil; ν_{max}(film)/cm^{-1} 1840 (C=O); δ_H 1.78–2.26 [11 H, m, 3-CH_3 and $(CH_2)_4$]; δ_C 22.0, 22.4, 24.0, 33.3, 35.8, 70.7, 98.0 and 168.5 (Found: C, 55.1; H, 6.7; Cl, 20.4. $C_8H_{11}ClO_2$ requires C, 55.0; H, 6.35; Cl, 20.3%).

(±)-3-Chloro-4,4-diethyl-3-methyloxetan-2-one 7Ac. Colourless oil; ν_{max}(film)/cm^{-1} 1838 (C=O); δ_H 0.97–1.03 (6 H, m, 2 × 4-CH_2CH_3), 1.86 (3 H, s, 3-CH_3), 1.88–1.98 (2 H, m, 4-CH_2CH_3) and 2.04–2.11 (2 H, q, *J* 7.4, 4-CH_2CH_3); δ_C 8.1, 8.2, 21.1, 24.9, 26.5, 72.9, 90.8 and 168.6 (Found: C, 54.5; H, 7.7; Cl, 20.1. $C_8H_{13}ClO_2$ requires C, 54.4; H, 7.4; Cl, 20.1%).

(±)-3-Chloro-3,4,4-trimethyloxetan-2-one 7Ad. Colourless solid, mp 66–70 °C; ν_{max}(CCl_4)/cm^{-1} 1839 (C=O); δ_H 1.62 (3 H, s, 4-CH_3), 1.69 (3 H, s, 4-CH_3) and 1.83 (3 H, s, 3-CH_3); δ_C 21.4, 22.8, 25.2, 72.6, 86.3 and 168.2 (Found: C, 48.65; H, 6.1; Cl, 24.0. $C_6H_9ClO_2$ requires C, 48.5; H, 6.1; Cl, 23.9%).

(3*R,4*R**)-3-Chloro-4-ethyl-3,4-dimethyloxetan-2-one *syn*-7Ae and (3*R**,4*S**)-3-chloro-4-ethyl-3,4-dimethyloxetan-2-one *anti*-7Ae.** Colourless oil, unseparated 1:1 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1838 (C=O); δ_H 1.03–1.09 (3 H, m, 4-CH_2CH_3), 1.56 (1.5 H, s, 4-CH_3), 1.66 (1.5 H, s, 4-CH_3), 1.83 (1.5 H, s, 3-CH_3), 1.86 (1.5 H, s, 3-CH_3) and 1.88–2.08 (2 H, m, 4-CH_2CH_3); δ_C 8.5, 8.7, 19.3, 20.8, 21.4, 27.8, 28.9, 30.9, 72.7, 72.8, 88.4, 88.9 and 168.4 (Found: C, 51.8; H, 6.9; Cl, 21.8. $C_7H_{11}ClO_2$ requires C, 51.7; H, 6.8; Cl, 21.8%).

(3*R,4*R**)-3-Chloro-3,4-dimethyl-4-phenyloxetan-2-one *syn*-7Af and (3*R**,4*S**)-3-chloro-3,4-dimethyl-4-phenyloxetan-2-one *anti*-7Af.** Separated 1:0.5 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1841 (C=O). Compound *syn*-**7Af**: colourless oil; δ_H 1.40 (3 H, s, 4-CH_3), 1.99 (3 H, s, 3-CH_3) and 7.26–7.46 (5 H, m, Ph); δ_C 23.6, 26.1, 74.2, 88.4, 124.4, 128.5, 128.8, 138.4 and 167.9 (Found: C, 62.5; H, 5.4; Cl, 16.5. $C_{11}H_{11}ClO_2$ requires C, 62.7; H, 5.3; Cl, 16.8%). Compound *anti*-**7Af**: colourless crystals, mp 50–52 °C; δ_H 1.92 (3 H, s, 4-CH_3), 1.96 (3 H, s, 3-CH_3) and 7.24–7.44 (5 H, m, Ph); δ_C 21.4, 24.2, 74.3, 88.4, 124.8, 128.3, 128.4, 139.4 and 167.8 (Found: C, 62.6; H, 5.6; Cl, 16.6. $C_{11}H_{11}ClO_2$ requires C, 62.7; H, 5.3; Cl, 16.8%).

(3*R,4*R**)-4-*tert*-Butyl-3-chloro-3-methyloxetan-2-one *syn*-7Ag and (3*R**,4*S**)-4-*tert*-butyl-3-chloro-3-methyloxetan-2-one *anti*-7Ag.** Colourless oil, unseparated 1:1.5 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1847 (C=O); *syn*-7**Ag**: δ_H 1.10 [9 H, s, 4-$C(CH_3)_3$], 1.90 (3 H, s, 3-CH_3) and 4.46 (1 H, s, 4-H); δ_C 20.7, 25.6, 33.7, 69.5, 93.5 and 167.8. *anti*-7**Ag**: δ_H 1.14 [9 H, s, 4-$C(CH_3)_3$], 1.91 (3 H, s, 3-CH_3), 4.13 (1 H, s, 4-H); δ_C 24.9, 27.1, 34.1, 68.3, 90.4 and 168.3 (Found: C, 54.4; H, 7.8; Cl, 20.0. $C_8H_{13}ClO_2$ requires C, 54.4; H, 7.4; Cl, 20.1%).

(3*R,4*R**)-3-Chloro-4-cyclohexyl-3-methyloxetan-2-one *syn*-7Ah and (3*R**,4*S**)-3-chloro-4-cyclohexyl-3-methyloxetan-2-one *anti*-7Ah.** Colourless oil, incompletely separated 1:1 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1835 (C=O); *syn*-**7Ah**: δ_H 0.90–1.95 (11 H, m, 4-C_6H_{11}), 1.81 (3 H, s, 3-CH_3) and 4.32 (1 H, d, *J* 10, 4-H); δ_C 19.2, 24.91, 24.94, 26.0, 28.0, 28.7, 38.8, 68.5, 89.9 and 168.3. *anti*-**7Ah**: δ_H 0.85–1.98 (11 H, m, 4-C_6H_{11}), 1.87 (3 H, s, 3-CH_3) and 4.03 (1 H, d, *J* 10, 4-H); δ_C 24.7, 24.9, 25.0, 26.1, 27.8, 28.4, 39.2, 70.7, 87.4 and 168.4 (Found: C, 59.9; H, 7.7; Cl, 17.85. $C_{10}H_{15}ClO_2$ requires C, 59.3; H, 7.5; Cl, 17.5%).

(3*R,4*R**)-3-Chloro-3-methyl-4-(2-phenylethyl)oxetan-2-one *syn*-7Ai and (3*R**,4*S**)-3-chloro-3-methyl-4-(2-phenylethyl)-oxetan-2-one *anti*-7Ai.** Colourless oil, unseparated 1:1 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1840 (C=O); δ_H 1.70 (1.5 H, s, 3-CH_3), 1.85 (1.5 H, s, 3-CH_3), 2.03–2.25 (2 H, m, CH_2), 2.72–2.86 (2 H, m, CH_2), 4.38–4.42 (0.5 H, m, 4-H, *anti*-**7Ai**), 4.63–4.67 (0.5 H, m, 4-H, *syn*-**7Ai**) and 7.18–7.34 (5 H, m, Ph); δ_C 19.0, 24.3, 30.9, 31.3, 32.1, 33.3, 69.1, 70.9, 83.1, 85.6, 126.7, 126.9, 128.65, 128.68, 128.9, 129.0, 139.8, 140.1, 167.8 and 168.1 (Found: C, 64.4; H, 6.1; Cl, 15.8. $C_{12}H_{13}ClO_2$ requires C, 64.15; H, 5.8; Cl, 15.8%).

(±)-3-Chloro-3-ethyl-1-oxaspiro[3.5]nonan-2-one 7Ba. Colourless oil; ν_{max}(film)/cm^{-1} 1835 (C=O); δ_H 1.19 (3 H, t, *J* 7, 3-CH_2CH_3), 1.58–1.82 (8 H, m, 4 × CH_2) and 1.98–2.30 (4 H, m, 2 × CH_2); δ_C 8.7, 22.4, 24.4, 26.0, 31.6, 34.0, 77.7, 87.9 and 168.1 (Found: C, 59.7; H, 7.4; Cl, 17.65. $C_{10}H_{15}ClO_2$ requires C, 59.3; H, 7.5; Cl, 17.5%).

(±)-3-Chloro-3-ethyl-1-oxaspiro[3.4]octan-2-one 7Bb.[17a] Colourless oil; ν_{max}(film)/cm^{-1} 1835 (C=O); δ_H 1.17–1.22 (3 H, t, *J* 7, 3-CH_2CH_3) and 1.77–2.27 (10 H, m, 5 × CH_2); δ_C 8.7, 23.0, 23.9, 28.0, 33.0, 36.2, 75.4, 98.0 and 168.0 (Found: C, 57.4; H, 7.4; Cl, 19.0. $C_9H_{13}ClO_2$ requires C, 57.3; H, 6.95; Cl, 18.8%).

(±)-3-Chloro-3,4,4-triethyloxetan-2-one 7Bc. Colourless oil; ν_{max}(film)/cm^{-1} 1834 (C=O); δ_H 0.86–0.98 (6 H, m, 2 × 4-CH_2CH_3), 1.08–1.15 (3 H, t, *J* 7, 3-CH_2CH_3) and 1.82–2.20 (6 H, m, 3 × CH_2CH_3); δ_C 8.1, 8.2, 8.9, 24.6, 26.3, 78.1, 91.1 and 168.1 (Found: C, 56.7; H, 8.1; Cl, 18.6. $C_9H_{15}ClO_2$ requires C, 56.7; H, 7.9; Cl, 18.6%).

(±)-3-Chloro-3-ethyl-4,4-dimethyloxetan-2-one 7Bd. Colourless oil; ν_{max}(film)/cm^{-1} 1837 (C=O); δ_H 1.08–1.15 (3 H, t, *J* 7, 3-CH_2CH_3), 1.56 (3 H, s, 4-CH_3), 1.63 (3 H, s, 4-CH_3) and 1.93–2.21 (2 H, m, 3-CH_2CH_3); δ_C 8.5, 22.7, 25.7, 27.0, 84.3 and 167.8 (Found: C, 51.6; H, 7.0; Cl, 21.7. $C_7H_{11}ClO_2$ requires C, 51.7; H, 6.8; Cl, 21.8%).

(3*R,4*R**)-3-Chloro-3,4-diethyl-4-methyloxetan-2-one *syn*-7Be and (3*R**,4*S**)-3-chloro-3,4-diethyl-4-methyloxetan-2-one *anti*-7Be.** Colourless oil, unseparated 1:1 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1835 (C=O); δ_H 0.92–1.15 (6 H, m, 2 × CH_2CH_3), 1.58 (1.5 H, s, 4-CH_3), 1.65 (1.5 H, s, 4-CH_3), 1.80–2.22 (4 H, m, 2 × CH_2CH_3); δ_C 8.5, 8.6, 8.9, 19.3, 21.7, 26.5, 27.0, 28.5, 31.1, 77.6, 77.8, 88.6, 89.0 and 168.0 (Found: C, 54.4; H, 7.6; Cl, 20.05. $C_8H_{13}ClO_2$ requires C, 54.4; H, 7.4; Cl, 20.1%).

(3*R,4*R**)-3-Chloro-3-ethyl-4-methyl-4-phenyloxetan-2-one *syn*-7Bf and (3*R**,4*S**)-3-chloro-3-ethyl-4-methyl-4-phenyloxetan-2-one *anti*-7Bf.** Colourless oil, separated 1:0.7 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1840 (C=O); *syn*-**7Bf** (less polar diastereoisomer): δ_H 0.96–1.04 (3 H, t, *J* 7, 3-CH_2CH_3), 1.52–1.63 (2 H, q, *J* 7.5, 3-CH_2CH_3), 1.99 (3 H, s, 4-CH_3) and 7.30–7.43 (5 H, m, Ph); δ_C 8.6, 26.3, 29.8, 78.9, 88.3, 124.7, 128.5, 128.8, 138.5 and 167.4 (Found: C, 64.2; H, 5.7; Cl, 16.0. $C_{12}H_{13}ClO_2$ requires C, 64.15; H, 5.8; Cl, 15.8%). *anti*-**7Bf** (more polar diastereoisomer): δ_H 1.23–1.30 (3 H, t, *J* 7, 3-CH_2CH_3), 1.93 (3 H, s, 4-CH_3), 2.21–2.36 (2 H, m, 3-CH_2CH_3) and 7.25–7.47 (5 H, m, Ph); δ_C 8.5, 24.2, 26.6, 78.9, 88.7, 124.9, 128.3 (2 signals), 139.5 and 167.4 (Found: C, 64.1; H, 5.9; Cl, 16.1. $C_{12}H_{13}ClO_2$ requires C, 64.15; H, 5.8; Cl, 15.8%).

(3*R,4*R**)-4-*tert*-Butyl-3-chloro-3-ethyloxetan-2-one *syn*-7Bg and (3*R**,4*S**)-4-*tert*-butyl-3-chloro-3-ethyloxetan-2-one *anti*-7Bg.** Separated 1:2 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1840 (C=O); *syn*-**7Bg** (crystalline diastereoisomer, mp 35–39 °C): δ_H 1.10 [9 H, s, 4-C$(CH_3)_3$], 1.24 (3 H, t, *J* 7, 3-CH_2CH_3), 2.02 (1 H, q, *J* 7, 3-CH_2CH_3), 2.44 (1 H, q, *J* 7, 3-CH_2CH_3) and 4.46 (1 H, s, 4-H); δ_C 9.3, 25.9, 26.3, 33.7, 74.7, 94.0 and 167.3 (Found: C, 56.9; H, 8.0; Cl, 18.8. $C_9H_{15}ClO_2$ requires C, 56.7; H, 7.9; Cl, 18.6%). *anti*-**7Bg** (colourless oil): δ_H 1.16–1.19 [12 H, s, 4-C$(CH_3)_3$ and t, *J* 7, 3-CH_2CH_3], 2.09–2.16 (2 H, q, *J* 7, 3-CH_2CH_3) and 4.11 (1 H, s, 4-H); δ_C 8.5, 25.1, 32.6, 33.9, 73.0, 89.0 and 168.1 (Found: C, 56.7; H, 8.1; Cl, 18.6. $C_9H_{15}ClO_2$ requires C, 56.7; H, 7.9; Cl, 18.6%).

(3*R,4*R**)-3-Chloro-4-cyclohexyl-3-ethyloxetan-2-one *syn*-7Bh and (3*R**,4*S**)-3-chloro-4-cyclohexyl-3-ethyloxetan-2-one *anti*-7Bh.** Colourless oil, partially separated 1:1.6 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1835 (C=O); *syn*-**7Bh**: δ_H 1.23 (3 H, t, *J* 7, 3-CH_2CH_3), 1.10–2.07 (12 H, m, 6 × CH_2), 2.24–2.36 (1 H, m, *tert*-H) and 4.33 (1 H, d, *J* 11, 4-H); δ_C 8.6, 24.96, 24.98, 25.8, 26.0, 28.1, 28.8, 38.3, 73.4, 90.2 and 167.6. *anti*-**7Bh**: δ_H 1.12 (3 H, t, *J* 7, 3-CH_2CH_3), 1.16–2.18 (13 H, m, 4-C_6H_{11} and 3-CH_2CH_3) and 4.04 (1 H, d, *J* 10, 4-H); δ_C 8.6, 24.9, 25.1, 26.1, 27.9, 28.5, 30.5, 38.9, 75.6, 85.9 and 168.2 (Found: C, 61.1; H, 8.0; Cl, 16.5. $C_{11}H_{17}ClO_2$ requires C, 61.0; H, 7.9; Cl, 16.4%).

(3*R,4*R**)-3-Chloro-3-ethyl-4-(2-phenylethyl)oxetan-2-one *syn*-7Bi and (3*R**,4*S**)-3-chloro-3-ethyl-4-(2-phenylethyl)oxetan-2-one *anti*-7Bi.** Colourless oil, separated 1:1 mixture of *syn* and *anti* diastereoisomers; ν_{max}(film)/cm^{-1} 1842 (C=O); *syn*-**7Bi**: δ_H 1.17 (3 H, t, *J* 7, 3-CH_2CH_3), 1.90–2.20 (4 H, m, 2 × CH_2), 2.70–2.91 (2 H, m, CH_2), 4.64–4.67 (1 H, dd, *J* 4 and 10, 4-H) and 7.19–7.34 (5 H, m, Ph); δ_C 8.4, 25.2, 31.4, 31.8, 85.8, 126.9, 128.8, 129.1, 129.9, 140.0 and 167.5 (Found: C, 65.6; H, 6.2; Cl, 14.7. $C_{13}H_{15}ClO_2$ requires C, 65.4; H, 6.3; Cl, 14.85%). *anti*-**7Bi**: δ_H 1.11 (3 H, t, *J* 7, 3-CH_2CH_3), 2.09–2.30 (4 H, m, 2 × CH_2), 2.73–2.81 (2 H, m, CH_2), 4.40–4.45 (1 H, dd, *J* 5 and 8, 4-H) and 7.19–7.35 (5 H, m, Ph); δ_C 8.5, 30.4, 30.9, 33.3, 75.6, 81.5, 126.7, 128.6, 128.8, 140.2 and 167.8 (Found: C, 65.7; H, 6.6; Cl, 14.9. $C_{13}H_{15}ClO_2$ requires C, 65.4; H, 6.3; Cl, 14.85%).

General procedure for the preparation of the α,α-dichloro-β-lactones 7C from phenyl 2,2-dichloroethanoate 1C and the carbonyl compounds 3

The preparation was performed in analogy to the foregoing general procedure with the following modification. Hexamethyldisilazane was used in all cases. The temperature for the preparation of the enolate and the reaction with the carbonyl compound was lowered to −110 °C. For work-up the reaction mixture was poured into 1 M aqueous hydrochloric acid (20 cm^3) and diethyl ether (50 cm^3). The organic phase was then washed with 1 M aqueous sodium hydroxide (2 × 7.5 cm^3) and dried. The β-lactones were obtained by flash chromatography. The yields of isolated products are given in Table 1 (entries 19–27). According to this general procedure the following α,α-dichloro-β-lactones **7C** have been prepared.

3,3-Dichloro-1-oxaspiro[3.5]nonan-2-one 7Ca.[18b] Colourless solid, mp 37–38 °C; ν_{max}(CCl_4)/cm^{-1} 1840 (C=O); δ_H 1.32–2.15 [10 H, m, $(CH_2)_5$]; δ_C 22.7, 24.1, 33.4, 85.3, 91.4 and 162.5 (Found: C, 46.1; H, 4.9; Cl, 33.7. $C_8H_{10}Cl_2O_2$ requires C, 46.0; H, 4.8; Cl, 33.9%).

3,3-Dichloro-1-oxaspiro[3.4]octan-2-one 7Cb. Colourless solid, mp 36–38 °C; ν_{max}(CCl_4)/cm^{-1} 1840 (C=O); δ_H 1.87–1.95 (4 H, m, 2 × CH_2), 2.09–2.17 (2 H, m, CH_2) and 2.29–2.40 (2 H, m, CH_2); δ_C 23.9, 35.6, 83.2, 101.7 and 162.4 (Found: C, 43.05; H, 4.3; Cl, 36.3. $C_7H_8Cl_2O_2$ requires C, 43.1; H, 4.1; Cl, 36.4%).

3,3-Dichloro-4,4-diethyloxetan-2-one 7Cc.[21c] Colourless oil; ν_{max}(film)/cm^{-1} 1840 (C=O); δ_H 1.06 (6 H, t, *J* 7.5, 2 × 4-CH_2CH_3), 2.10 (4 H, q, *J* 7.5, 2 × 4-CH_2CH_3); δ_C 8.1, 26.3, 85.3, 94.5 and 162.4 (Found: C, 42.7; H, 5.2; Cl, 35.7. $C_7H_{10}Cl_2O_2$ requires C, 42.7; H, 5.1; Cl, 36.0%).

3,3-Dichloro-4,4-dimethyloxetan-2-one 7Cd.[18b,19] Colourless solid, mp 26 °C; ν_{max}(CCl_4)/cm^{-1} 1845 (C=O); δ_H 1.78 (6 H, s, 2 × 4-CH_3); δ_C 24.5, 85.4, 90.2 and 162.1 (Found: C, 35.5; H, 3.5; Cl, 41.9. $C_5H_6Cl_2O_2$ requires C, 35.5; H, 3.6; Cl, 42.0%).

(±)-3,3-Dichloro-4-ethyl-3-methyloxetan-2-one 7Ce.[18b] Colourless oil; ν_{max}(film)/cm^{-1} 1845 (C=O); δ_H 1.11 (3 H, t, *J* 7, 4-CH_2CH_3), 1.73 (3 H, s, 4-CH_3) and 2.05–2.13 (2 H, m, 4-CH_2CH_3); δ_C 8.6, 21.0, 30.3, 85.4, 92.5 and 162.3 (Found: C, 39.5; H, 4.4; Cl, 38.7. $C_6H_8Cl_2O_2$ requires C, 39.3; H, 4.4; Cl, 38.7%).

(±)-4-*tert*-Butyl-3,3-dichlorooxetan-2-one 7Cg. Colourless oil; ν_{max}(film)/cm^{-1} 1850 (C=O); δ_H 1.18 [9 H, s, 4-C$(CH_3)_3$] and 4.59 (1 H, s, 4-H); δ_C 24.7, 34.4, 79.8, 95.4 and 161.8 (Found: C, 42.95; H, 4.95; Cl, 35.9. $C_7H_{10}Cl_2O_2$ requires C, 42.7; H, 5.1; Cl, 36.0%).

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