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SmI_2-Mediated 3-*exo*-trig cyclisation of δ-oxo-α,β-unsaturated esters to cyclopropanols and derivatives

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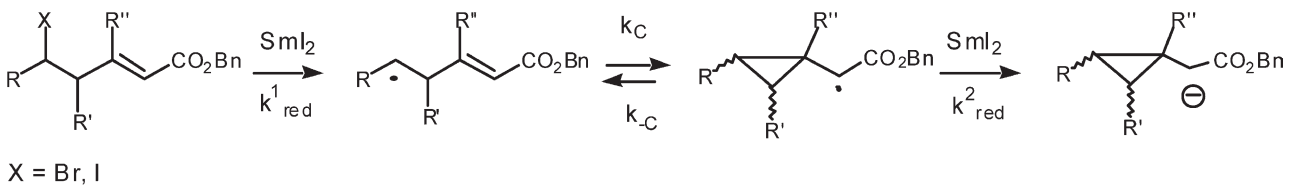
Abstract—In the presence of samarium diiodide and a proton source, δ-oxo-γ,γ-disubstituted-α,β-unsaturated esters of general formula R–CO–C(R′,R′)–CH=CH–CO_2Bn readily cyclise to *trans*-cyclopropanol products and/or lactones derived from the *cis* isomers. For R=aryl, good stereoselectivities (ca 90%) in favor of the alcohols are generally obtained while a mixture of alcohols and lactones is obtained with R=alkyl or H. For R=cyclopropyl, the lactone is exclusively obtained in more than 90% yield. A mechanistic rationalisation of these variations of diastereoselectivity is proposed.

1. Introduction

In the past 20 to 30 years, radical cyclisations have been extensively used, often with great success, for obtaining carbocycles, especially five-membered and to a lesser extent six-membered ring systems. Meanwhile, few radical cyclisations have been described, which lead to cyclopropanes. This paucity of results is easily accounted for by the fact that, contrary to 5-*exo*-trig cyclisations which are usually fast and irreversible, 3-*exo*-trig radical cyclisations, albeit kinetically feasible, are on the other hand usually thermodynamically strongly disfavored. Indeed, in the parent system, cyclisation of the homoallyl radical is somewhat 10^4 times slower ($k_C=1.0\times10^4\ s^{-1}$ vs $k_{-C}=1.3\times10^8\ s^{-1}$ at 25 °C)[1] than reopening of the cyclopropylmethyl radical. As a result, only homoallylic systems with very specific features have been successfully cyclised to cyclopropane molecules under exclusive radical conditions. Such specific features include structural constraints[2] or the presence of groups able, once the cyclopropylcarbinyl radical is formed, either to stabilise it[3] or to involve it into further fast radical reactions such as cyclisations[2e,f] (cascade processes) or fragmentations (β-elimination of thiyl group).[4]

A few years ago, we reported that δ-bromo and δ-iodo-α,β-unsaturated esters could be cyclised to cyclopropane compounds in the presence of two equivalents of samarium diiodide and a proton donor (typically *tert*-butanol).[5] The success of this procedure was attributed to the known ability of SmI_2 to promote radical-anionic tandem reactions, a property that has extensively been used for various synthetic purposes.[6a,b] In our case, the following mechanism has been proposed[5] (Scheme 1): the homoallylic radical initially formed by monoelectronic reduction of the starting halide cyclises to α-carbalkoxy-substituted cyclopropylcarbinyl radical. Despite the presence of the carbalkoxy substituent, kinetic measurements have shown that this equilibrated process is still in favor of the open radical form, albeit to a lesser extent than in the parent system (k_c/k_{-c}=ca 10).[7] This, however, is of no consequence as the displacement of the overall reaction towards cyclisation is ensured by



Scheme 1.

Keywords: Samarium diiodide; Radical cyclisations; Cyclopropanols; Ketyl radicals.
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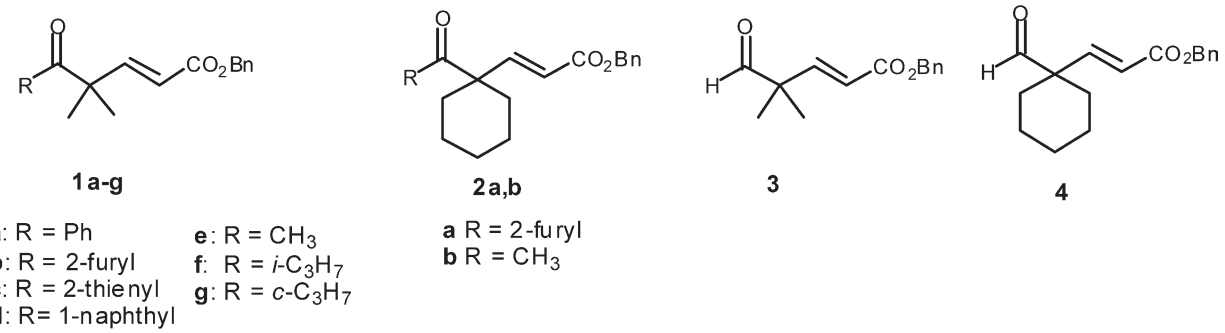
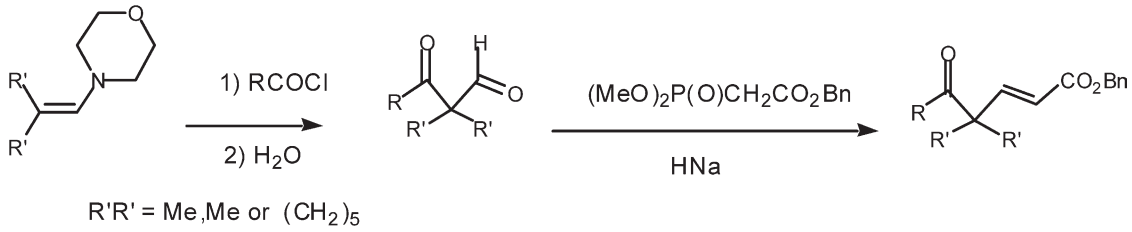


Figure 1.



Scheme 2.

subsequent and irreversible facile monoelectronic reduction of the cyclopropylcarbinyl radical to the corresponding enolate.[†] We later showed[8] that considerable racemisation was observed in the cyclisation of enantioenriched δ-halo-α,β-unsaturated esters bearing a substituent at the γ-position. Such racemisation was accounted for by assuming that reopening of the cyclopropylcarbinyl radical is probably faster that its reduction to enolate ($k_{-c}>k^2_{red}$ [SmI_2] in Scheme 1).

Notwithstanding the racemisation problem, the SmI_2 mediated cyclisation of δ-halo-α,β-unsaturated esters was found to tolerate the presence of various substituents at the β, γ and δ positions (α-position was not tested in this respect). Unfortunately, the diastereoselectivities of these reactions are low and mixtures of *cis* and *trans* substituted cyclopropanes were usually obtained in comparable amounts. We then turned our attention to the cyclisation of δ-oxo-α,β-unsaturated esters as a way to obtain cyclopropanols through formation of the corresponding ketyl radicals and their subsequent intramolecular addition on the double bond. It was hoped that better diastereoselectivities would be attained in these reactions. Indeed, many examples of related SmI_2 promoted 5-*exo*-trig, 6-*exo*-trig and even 4-*exo*-trig cyclisations of ζ- η- and ϵ-oxo-enoates respectively can be found in the literature. These reactions often display very good stereoselectivities[9] due to the fact that in the transition state, the C–O bond of the ketyl radical and the C=C bond conjugated to the carbalkoxy group adopt preferentially, for stereoelectronic reasons, an antiparallel relationship.[10] Steric effects or coordination to samarium of various functional groups in the substrate molecule may however complicate the stereochemical issue.[11]

A preliminary communication on the cyclisation of δ-oxo-α,β-unsaturated esters had already been issued[12] essentially dealing with aldehydic substrates. We present here a full report of our work which includes aromatic and alkyl ketones. For reasons that will be later specified some cyclisations of aldehydic compounds were also reinvestigated. Several results given in our preliminary communication were thus found erroneous and have been consequently revised.

2. Results

2.1. Synthesis of substrates for cyclisation

In order to avoid any complication which could arise from accidental migration of the double bond from α,β to β,γ position, we have limited our studies to γ,γ-disubstituted δ-keto enoates of general formula **1**–**4** (Fig. 1) Those include aromatic substrates **1a**–**d** and **2a**, alkyl ketones **1e**–**g** and **2b** and aldehydic compounds **3** and **4**. Most ketonic substrates were synthesized by the two-step procedure of Scheme 2. In the first step, acylation of morpholino-enamines derived from isobutyraldehyde or cyclohexane–carboxaldehyde with the appropriate acyl chloride followed by hydrolytic work-up, as described by Inukai and Yoshigawa,[13] gave the corresponding β-keto-aldehydes. In a second step, Wadsworth–Emmons condensation under standard conditions with benzyl dimethoxyphosphono-acetate gave the desired products. Probably due to more severe steric crowding, acylation of isobutyraldehyde morpholino-enamine with isobutyryl chloride and with naphthoyl chloride gave very poor results.

[†] An analogous radical–anionic tandem process has been proposed to explain the formation of cyclopropyl ring in some nickel complex catalysed electroreductive cyclisations: Ozaki, S.; Matsui, E; Waku, J.; Ohmori, H. *Tetrahedron Lett*. **1997**, *38*, 2705–2708. See also Gassman, P. G.; Lee, C. J. *J. Am. Chem. Soc.*, **1989**, *111*, 739–740.

At this point of our investigation, we became aware of another publication[14] showing that acylation of pyrrolidino-enamines takes place much more readily than that of morpholino-enamines. Indeed, acylation of isobutyraldehyde pyrrolidino-enamine with 1-naphthoyl chloride gave after hydrolytic work-up the desired β-keto-aldehyde in very satisfactory yield. As to 3-oxo-2,2,4-trimethyl-pentanal, on the way to **1f**, it was prepared by aldol autocondensation of isobutyraldehyde in fair yield[15] followed by oxidation with PCC.

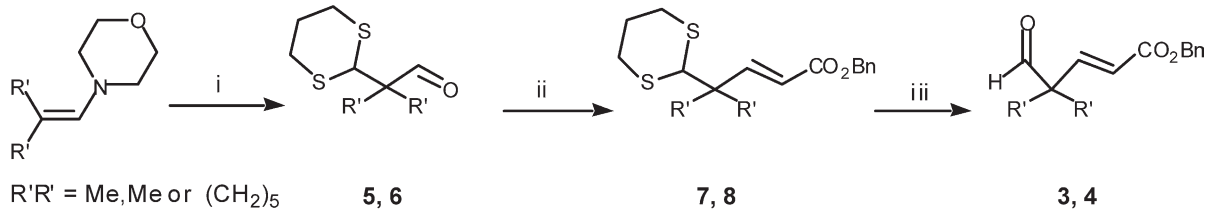
As reported in our preliminary communication, the aldehydic substrates **3** and **4** were prepared in three steps. Morpholino-enamines derived from isobutyraldehyde or cyclohexane–carboxaldehyde were first alkylated with 2-chloro-1,3-dithiane.[16] Hydrolytic work-up gave dithiane aldehydes **5** and **6** that were submitted to Wadsworth–Emmons olefination. The latent aldehydic function was finally unmasked by hydrolysis of the dithiane group in water/acetone in the presence of methyl iodide and collidine[17] (Scheme 3).

2.2. Cyclisations: procedure and experimental results

SmI_2-mediated cyclisations were conducted under inert (argon) dry atmosphere. The procedure was generally as follows: a 0.2 M solution of substrate in THF also containing 4 equiv. of *tert*-butanol was cooled to 0 °C. 2.2 equiv. of a 0.1 M solution of SmI_2 in THF was added dropwise through a cannula over a period of approximately 2 min. The reaction mixture was then stirred at room temperature for several (usually four to twelve) hours until TLC analysis on aliquots showed total consumption of the substrate. The reaction mixture was then quenched with dilute aqueous HCl. After standard work-up, the crude residue was first analysed by NMR and then submitted to column chromatography in order to isolate pure compounds. For a number of substrates, the reaction was carried out twice with different batches of SmI_2 solution with good reproducibility. Experimental procedures other than that described above—especially inverse addition and reactions carried out in the additional presence of four equivalents of HMPA—were also sometimes investigated. Since no significant differences in the outcome of the reaction were observed, they are not reported here.

In most cases only products of reductive cyclisation (Fig. 2) were obtained in our experiments. However, uncyclised products of direct reduction of the carbonyl (alcohol **9**) or of direct reduction of the carbon–carbon double bond (saturated ester **10**) were also found, in minor amounts, in the reaction of methyl ketone **2b** and isopropylketone **1f** respectively. In no cases could products of pinacol coupling be detected. Products of reductive cyclisation were cyclopropanols **11** in which the hydroxyl group and the carbalkoxymethyl group are *trans* to each other relatively to the cyclopropane ring and/or lactones **12** undoubtedly originating from lactonisation of the preliminary formed *cis* stereoisomeric cyclopropanol adducts. In the following of the text, stereoisomers **11** will be referred to as '*trans* cyclopropanols'. On NMR spectra, the methylene protons α to carbonyl of lactones **12** display a very characteristic *AB*X system made of one doublet and one doublet of doublets (J_{AB}=ca 18 Hz, J_{AX}=ca 7 Hz, J_{BX}=0 Hz) while cyclopropanols **11** display the usual pair of doublets of doublets ($J_{BX}\neq 0$ Hz).

The main results of our investigations are summarised in the table. On the NMR spectra of the crude reaction products, only two benzylic signals usually showed up, one corresponding to the *trans* cyclopropanol adduct and the other to benzyl alcohol. If we assume that all benzyl alcohol comes from lactonisation of the primarily formed *cis* cyclopropanol adduct, the *anti*/*syn* selectivity can also be deduced from the relative intensity of the NMR benzylic peaks. In the table, we have therefore reported both *anti*/*syn*



Scheme 3.

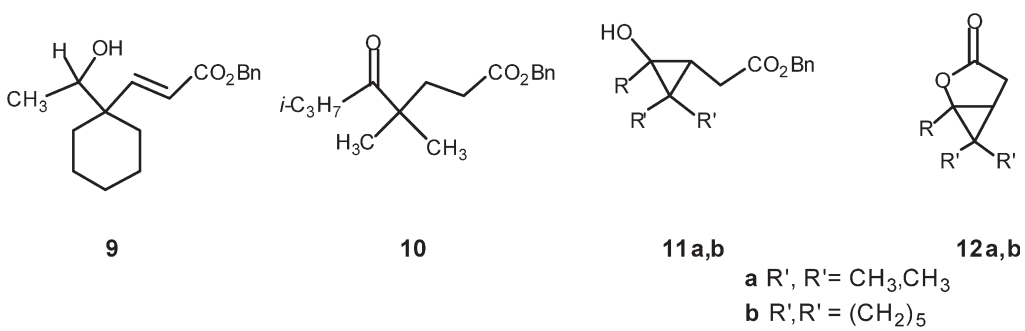
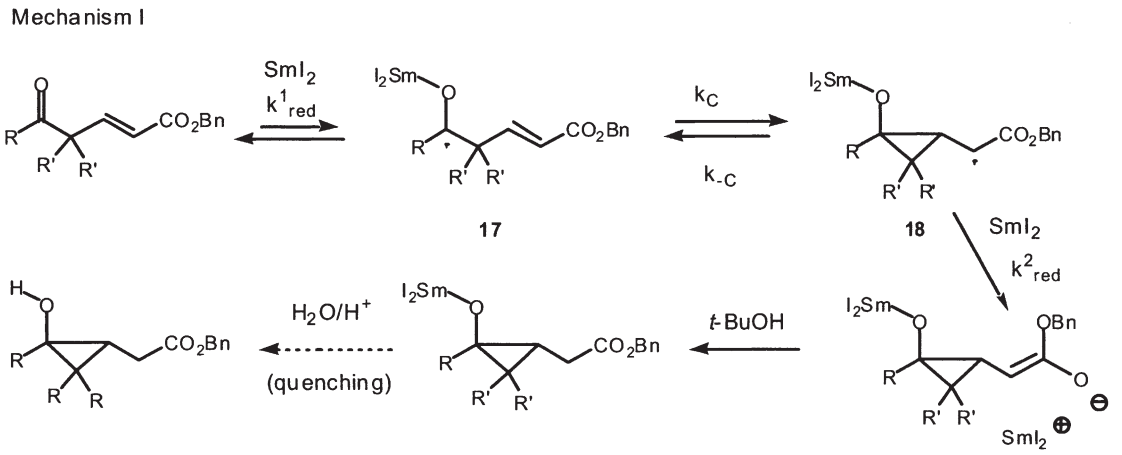


Figure 2.



Scheme 4.

selectivities deduced on the one hand from the respective amounts of *trans* cyclopropanol and lactone isolated by chromatography and on the other hand from NMR of the crude reaction mixture. A fair agreement between the two values was generally observed.

Aromatic ketonic substrates (entries 1–4) were found to give usually in high yield and with complete or very high stereoselectively *trans* cyclopropanols and only small amounts of lactones. With the more sterically encumbered 1-naphthyl substrate **1d** however, the proportion of lactones becomes important (entry 5). Concerning the cyclisation of alkyl ketonic compounds (entries 6–8), a mixture of lactone and of *trans*-cyclopropanol in comparable amounts was obtained not only with isopropyl ketone **1f** but even with the less sterically demanding methyl ketone **1e** and **2b**. Surprisingly, exclusive formation of the lactone in close-to-quantitative yield was observed with the cyclopropyl compound **1g** (entries 9a–c).

Given the results obtained above with non-aromatic ketones, we decided to reinvestigate the cyclisation of some aldehydes because our previous observations that cyclisation takes places with exclusive *anti* selectivity seemed now dubious. Indeed, in this reinvestigation, we found that these substrates also lead to a mixture of *trans* cyclopropanols and of lactones (entries 10, 11). We also found that the yields of the reactions was somewhat poorer than with ketonic compounds, but neither uncyclised products of direct reduction, nor products of pinacol coupling were detected.

3. Discussion

In our opinion, the collection of results presented here is too limited to allow for a complete understanding of the mechanisms by which δ-oxo α,β-unsaturated esters cyclise in the presence of SmI_2. We will therefore limit ourselves to some broad comments and mechanistic proposals must be considered more as working hypotheses for further investigation rather than as definite statements.

Reduction of ketones to ketyl radicals is notoriously thermodynamically much more favorable with aryl than with alkyl ketones. From a kinetic point of view, recent rate constant measurements with SmI_2 as the one electron reducing agent have shown that the reaction is 10^4 more rapid with acetophenone than with 2-butanone.[18] On the basis of these considerations, the following mechanism (mechanism I, Scheme 4) may be proposed for cyclisation of our arylic substrates. The keto group is first reduced most probably in a reversible way[18,19] to ketyl radical **17** which then adds to the double bond to give the cyclopropylcarbinyl radical **18**.‡ Further reduction to enolate by a second molecule of SmI_2 followed by protonation completes the reaction. Mechanism I is therefore akin to the one proposed earlier by ourselves for the cyclisation of δ-halo-α,β-unsaturated esters (see Scheme 1). It also corresponds to what is generally invoked for SmI_2 promoted intermolecular condensation of conjugated enoic esters with carbonyl compounds[20] and, as already mentioned, for SmI_2 promoted 4-*exo*, 5-*exo* and 6-*exo*-trig cyclisations of ϵ-,ζ- and η-oxo-enoates.[9] Therefore, in the present 3-*exo*-trig cyclisations, the *anti* stereoselectivity observed with substrates **1a–c** and **2a** could likewise be the result of a preference for a *trans* relationship of the C–O bond of the ketyl radical and the carbon–carbon double bond of the enoate moiety in the transition states of cyclisation (Fig. 3, **A** preferred to **B**). However, an essential difference between 3-*exo*-trig cyclisations and 5- and 6-*exo*-trig-cyclisations is that the former are reversible while the latter are not.§ As a result, in

‡ It is thus assumed that cyclisation takes place at the radical stage. A reaction sequence involving first two-electron reduction of the carbonyl group and then cyclisation cannot be totally ruled out. However, the fact that the cyclisation reactions are carried out in the presence of a proton donor renders improbable a cyclisation at an anionic stage. For other arguments in disfavor of anionic cyclisations (including the case where the initial two-electron reduction occurs at the carbon–carbon double bond of the enoate moiety instead of carbonyl) see Ref. 5 and references cited therein.

§ 4-*exo*-trig cyclisations are potentially reversible but the k_{-c} constant for ring opening of cyclobutyl methyl ketyl radical (2.5×10^4 s^{-1} at 25 °C) is at least three orders of magnitude smaller than that for cyclopropyl methyl ketyl radical.[23] Therefore, the probability for a rapid equilibration between open and cyclised radicals in samarium promoted reductice cyclisation of ϵ-oxo-α,β-unsaturated esters [9a–f] appears low. An isolated example of reductive opening by SmI_2/DMPU, of an α-ketocyclobutane ring within a fused tricyclic system, has been reported (Comins, D. L.; Zheng, X. *J. Chem. Soc.Chem. Commun.* **1994**, 2681–2682). Probably, in this rigid structure, the fragmentation process is greatly facilitated by favorable orbital overlapping.

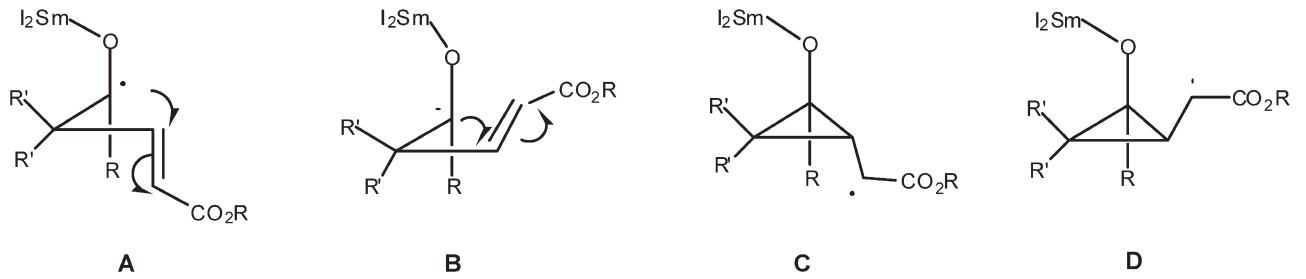


Figure 3.

our case the argument based on stereoelectronic preferences in the transition state of cyclisation holds true only if the retrocyclisation process is slow compared to the irreversible reduction of cyclopropylcarbinyl radical to enolate ($k_{-c} \ll k_{red}^2$ [SmI_2] in Scheme 4). In the reverse limit case ($k_{-c} \gg k_{red}^2$ [SmI_2]), application of the Curtin–Hammet principle[21] leads to the conclusion that the *anti/syn* selectivity depends now on the relative energy of the transition states leading from the *trans* and *cis* cyclopropylcarbinyl radicals **C** and **D** to the corresponding enolates. As pointed out in our preliminary communication,[12] the *trans* (*anti*) selectivity could then be explained by the development of strong repulsive electronic interactions during the reduction of the *cis* radical **D** to carbanion. At the present time of our investigation, it is difficult to ascertain which one (if any) of these two situations prevails. But the second one (fast equilibrium between homoallylic and cyclopropylcarbinyl radicals before further reduction to enolate) seems to us more in keeping with our past results on the cyclisation of δ-halo-α,β-unsaturated esters[8] (*vide supra*) as well as with the relative ease of formation and stability of aromatic ketyl radicals. It may be recalled that the ring opening of (2-phenylcyclopropyl)methyl radical **13** (Fig. 4) is among the fastest radical reactions calibrated to date with $k_{-c}=1.6\times10^{11}$ s^{-1} at 20 °C.[22] To the best of our knowledge, no kinetic data are available at the present time concerning the ring opening of 2-phenylcyclopropyl methyl ketyl radical **14**. Meanwhile ring opening of (2-phenylcyclopropyl) phenyl ketyl radical **15** is at least 10^5 to 10^6 faster than that of cyclopropyl phenyl ketyl radical **16** ($k_{-c}=3\times10^5$ to 3×10^6 s^{-1} vs ≤ 2 s^{-1} at 25 °C).[23]

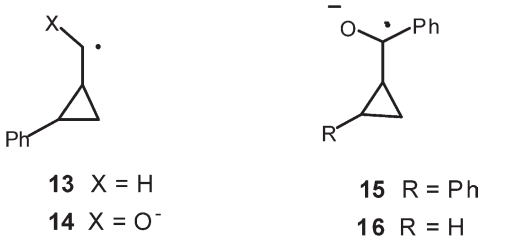
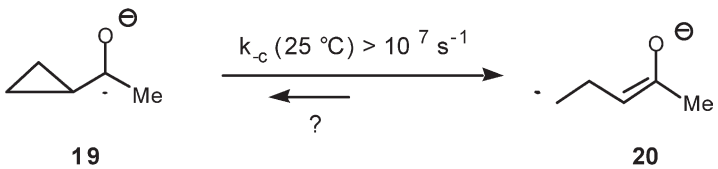


Figure 4.

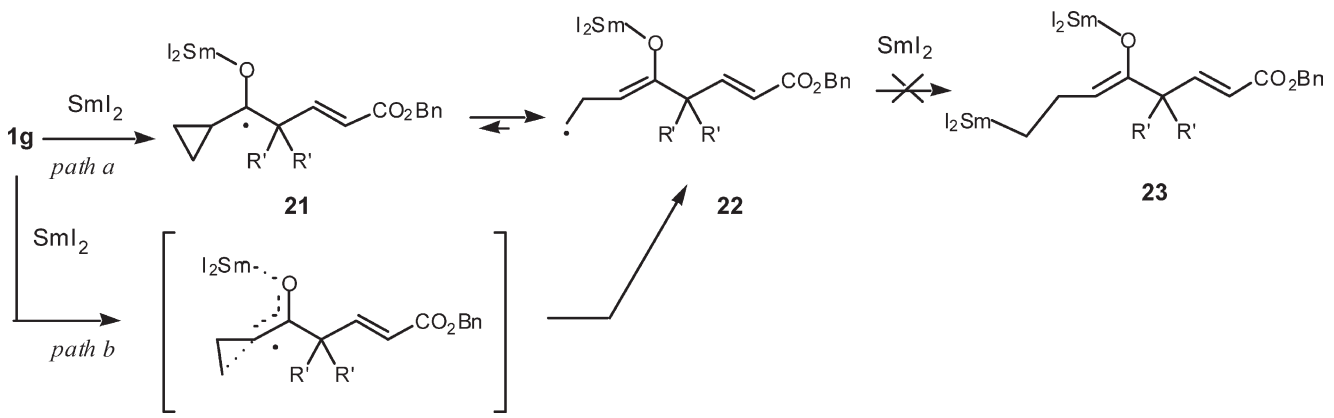
The increase in the proportion of lactone in the cyclisation of the 1-naphthyl substrate **1d** must be the result of steric effects that may be of two kinds: direct in favouring the formation of the less crowded *cis* cyclopropanol adduct, indirect in preventing coplanarity of the aromatic ring and the ketonic group due to unfavorable steric interactions between the *peri*-hydrogen of the naphthyl group with the carbonyl group on one side and with the *gem*-dimethyl group on the other side. Compound **1d** would thus react more like an alkyl ketonic compound than like an aryl ketonic compound.[24]

A most intriguing result of our investigation concerns the total selectivity observed in favor of the formation of lactone in the case of the cyclopropylketone substrate **1g**. The cyclisation of this substrate in which a potential cyclopropylcarbinyl-homoallyl type rearrangement is used as a radical probe was undertaken in the hope that it could be give helpful information as to the mechanism of cyclisation. Other examples of utilization of such cyclopropyl radical probes in SmI_2 mediated reactions may be found in the literature.[9e–f,25]

In a recent work,[23] Tanko and co-workers have shown that cyclopropyl-methyl ketyl radicals **19** rapidly open into distonic radical anion **20** with a k_{-c} constant at least equal to and probably higher than 10^7 s^{-1} (25 °C) (Scheme 5). Several examples of ring opening of cyclopropylketones in the presence of one electron reducing system such as Li in NH_3[26] or SmI_2[25a,25c,27] or under photon induced electron transfer[28] may be found in the literature. In our case, we may expect that monoelectronic reduction of the carbonyl group is immediately followed by or takes place concomitantly with (vide infra) ring opening leading to distonic radical **22** (Scheme 6). Probably due to a strong preference for *Z* configuration of the enolate double-bond (the *E*-isomer could cyclise in a 6-*exo*-trig fashion on the enoate moiety), **22** cannot undergo further chemical transformations other than reduction to a homoallylic organosamarium species **23** by a second molecule of SmI_2. Obviously this second reduction does not take place *under our conditions* since we do not observe the corresponding protonated adduct. In other words, in the case of cyclopropyl substrate **1g** the ketyl



Scheme 5.

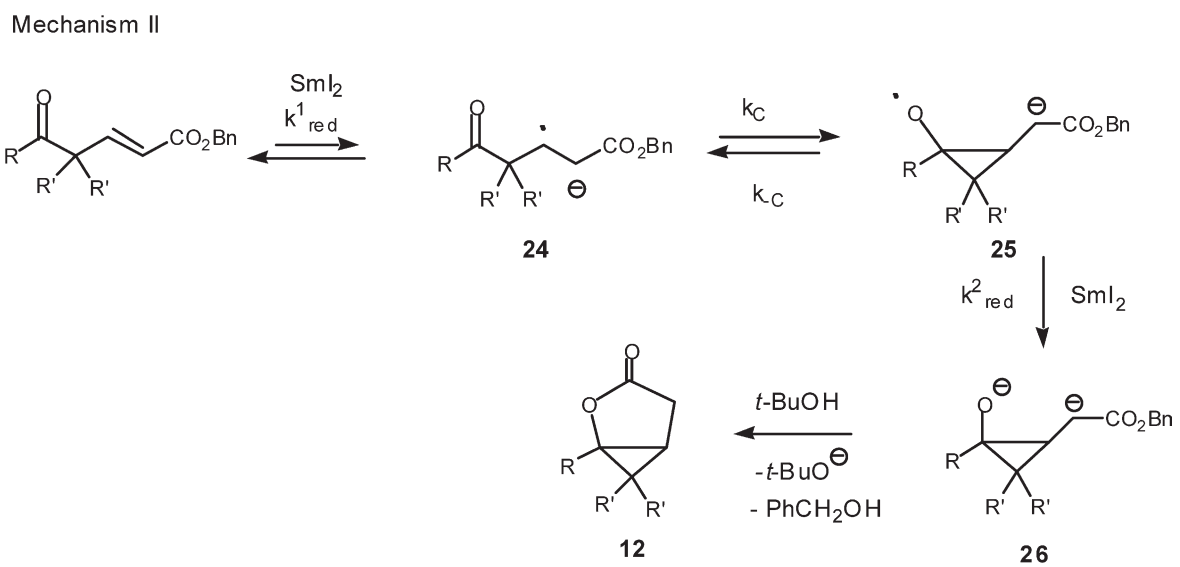


Scheme 6.

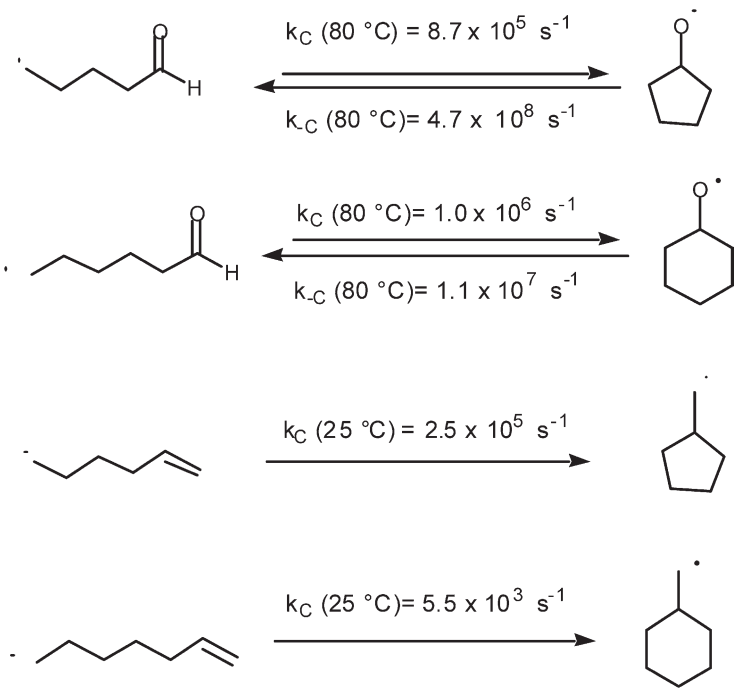
radical pathway is unproductive. We therefore propose for cyclisation of the cyclopropyl substrate a mechanism (mechanism II, Scheme 7) which starts with one electron reduction of the enoate moiety to radical anion **24**. Subsequent radical 3-*exo*-trig cyclisation on the carbonyl group leads to the cyclopropanoxy radical **25**. Finally, reduction of the cyclopropanoxy radical to dianion **26** could be extremely fast, thus displacing the reaction towards cyclisation. The reason why this cyclisation takes place with *syn* selectivity, leading ultimately to lactone **12** will be discussed later.

Before discussing mechanism II in some more details, it should be clearly stated that the proposal of a switch from mechanism I to mechanism II for cyclisation of cyclopropylketone **1g** on the ground that the ketyl radical pathway would now be unproductive relays on two assumptions that would need confirmation. The first one is that ring opening to distonic radical **22** is a reversible process. Reversibility of cyclopropane ring opening in the case of *aryl* cyclopropyl ketyl radical is well established.[23,29] This even includes[23,29b,] aryl cyclopropyl ketones bearing an extra phenyl group at the 2-position of cyclopropane (i.e., **15**, Fig. 4) despite the fact that such substitution induces stabilization of the open distonic form. On another hand, no data concerning putative reversibility of ring opening of *alkyl* cyclopropyl ketyl radical is available at the present time. The second one is that one-electron reduction of the carbonyl group and opening to distonic radical **22** by C–C bond breaking should in some way be concerted (Scheme 6, path b). Indeed, in the case of a stepwise mechanism going through the formation of a discrete ketyl radical **21** (path a), the existence of a further equilibrium between **21** and distonic radical **22** is not supposed to affect the *relative* proportions of ketyl radical **21** and radical anion **24**. Therefore, the reversible formation of **22** should not induce cyclopropyl ketone **1g** to cyclise according to mechanism II rather than mechanism I. Recent electrochemical investigations by Tanko and co-workers,[23] however, have led these authors to consider the stepwise mechanism as more probable.

Concerning now the plausibility of mechanism II itself and in support of it, α,β-unsaturated esters are known to be easily reduced by SmI_2 to radical anions. Those, in turn, can be further reduced to saturated esters[30] or give homo coupling products in dependance of the exact reaction conditions.[31] Intramolecular coupling involving 3-*exo* and



Scheme 7.



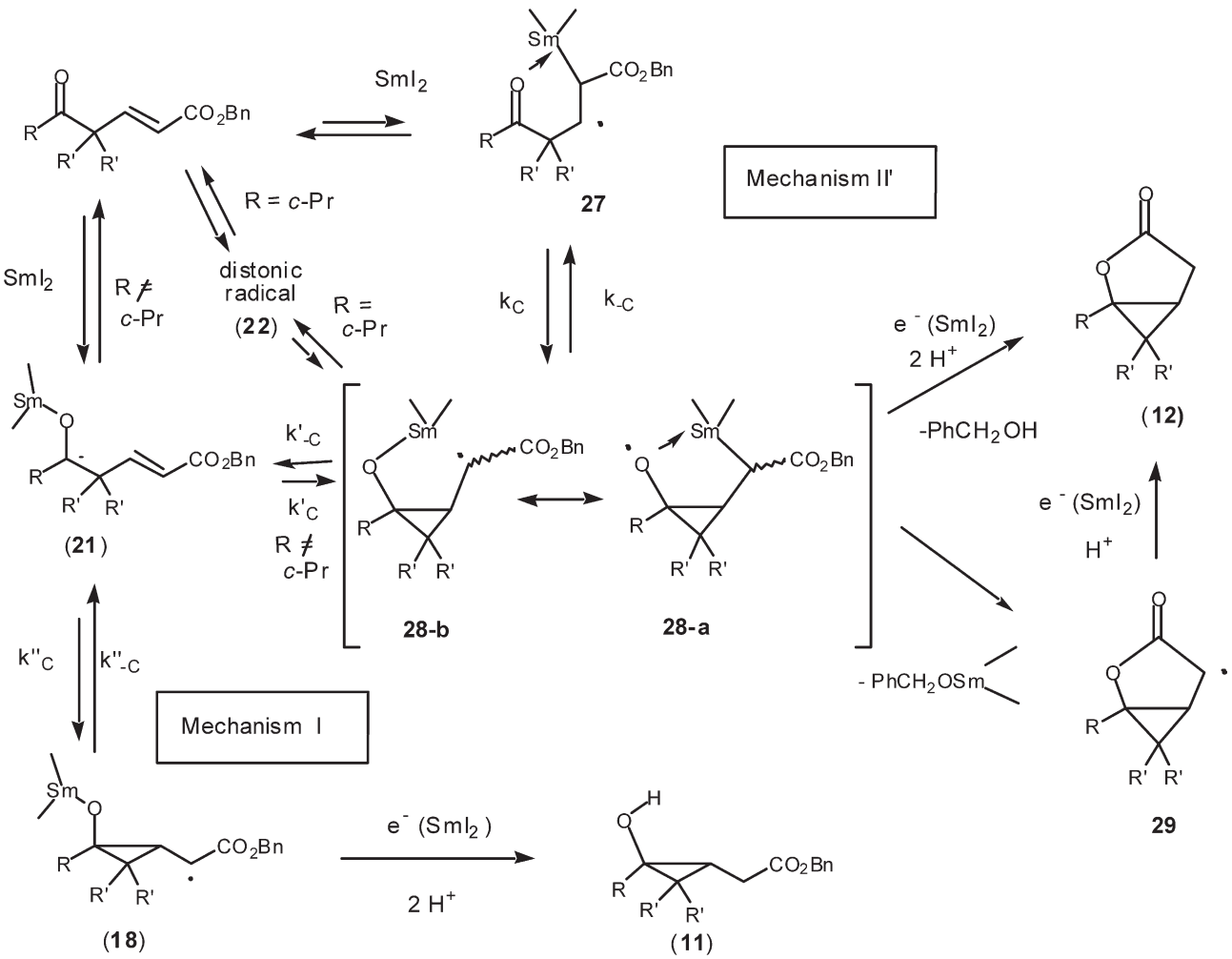
Scheme 8. [33]

6-*exo*-trig cyclisations of bis-enoates have also been reported.[31a] On a different ground, additions of alkyl radical onto carbonyl groups constitute a well-documented class of reactions, even if their utilisation for synthetic purpose[32] is much more limited than radical additions on ethylenic double bonds. This fact can be readily explained by comparison of kinetic data[33] concerning 5- and 6-*exo*-trig cyclisations of ethylenic and aldehydic parent systems as represented in Scheme 8. In both cases, reactions are fast but in the case of carbonyl compounds, the process is less favorable because they are reversible with a k_{-c} cycloreversion constant substantially higher than k_c. To the best of our knowledge, no kinetic data concerning either cyclisation of 3-oxo-propyl radical to cyclopropanoxy radical or cycloreversion of the latter species are available in the literature. However it may be inferred that this equilibrium, if it does take place, is largely displaced towards the open form. This of course is not in favor of mechanism II. It should nevertheless be noted that the formation of cyclopropanoxy radical have been postulated in other radical transformations for instance in the tin induced ring expansion of α-halomethyl[34] or other[35] ketones or in some tin induced 1,2 group migrations within radical species that are related to coenzyme B_{12} mediated rearrangements.[36,¶] Samarium diiodide[37] and more recently zinc and indium powder mediated[38] ring expansion of α-halomethyl cyclic β-keto esters have also been reported but in these cases it is difficult to decide whether these reactions truly involve the formation of cyclopropanoxy intermediates or follow an ionic pathway.

The main problem associated with mechanism II lays in the difficulty to account for *syn* selectivity. We may suspect that, as it is often the case, chelation of samarium plays a crucial role. We tentatively propose mechanism II′ being well aware of its speculative character. Mechanism II′, as represented in the right upper part of Scheme 9 is a further elaboration of mechanism II in which problems of stereochemistry and of coordination to samarium are more specifically addressed. Cyclisation of radical anion **27** under chelation control leads to the cyclopropanoxy radical **28a** tautomeric with the α-carbalkoxy substituted radical form **28b**. **28a**,**b** may undergo cycloreversion back to **27** or to ketyl radical **21** when R≠cyclopropyl. When R is cyclopropyl this last process is replaced by double cycloreversion back to distonic radical **22** which do not react further. Reduction to the dianionic species therefore seems the only possible evolution for the cyclopropyl substrate. After subsequent lactonisation–protonation in situ and/or during work-up, lactone **12** is finally produced. Alternatively, lactonisation may take place within **28a**,**b** to give **29** thus locking at this stage the molecule in the *cis* configuration.

The obtention of mixtures of *trans* cyclopropanols and lactones with aldehyde and alkyl ketone substrates could signify that both mechanisms I and II′ take place concurrently. If so, an additional supposition must however be made for the sake of consistency. Since ketyl radical **21** is the starting point of mechanism I, cycloreversion of **28-a**,**b** to **21** must not be too fast as compared to its further reduction to **12** or its lactonisation to **29**. Otherwise,

¶ Moreover, as pointed out by Curran,[25a] the alkoxy radical is likely to exist not as a free species, but coordinated to samarium(III) as represented in Scheme 9, species **28a** (vide infra). By further electron transfer from samarium, **28a** may also be seen[25a] as a carbo-alkoxy dianionic organic entity coordinated to samarium(IV).



Scheme 9.

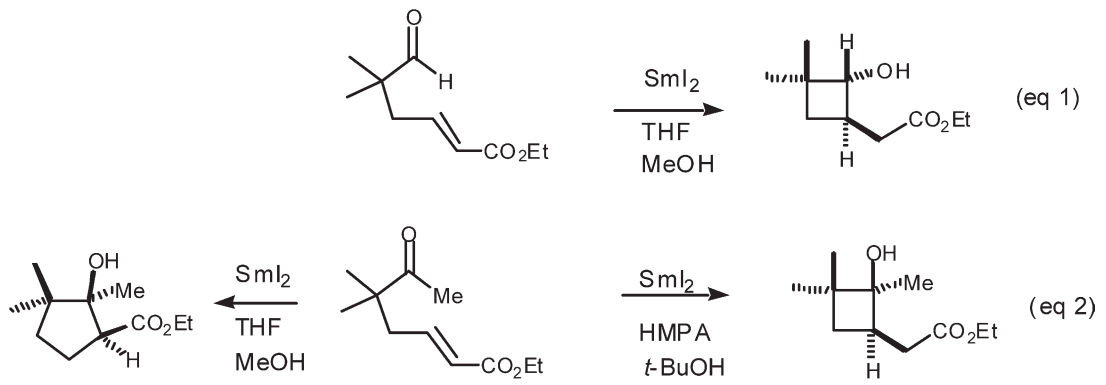
mechanism I (Schemes 4 and 9, left lower part) would ultimately operate.[‖]

The (partial) change of mechanism on going from aromatic ketones to aldehydes and alkyl ketones would reflect the less favorable formation of the ketyl radical. Interestingly an analogous change of mechanism—but this time on going from aldehydes to alkyl ketones—has been proposed by Procter and co-workers in the samarium mediated cyclisation of ϵ-oxo-α,β-unsaturated esters in THF/MeOH.[9e] According to the authors, aldehydic compounds (Eq. 1, Scheme 10) that lead to cyclobutanols with complete *anti*-selectivity, cyclise by addition of the ketyl radical onto the enoate moiety, i.e. according to mechanism I. In the case of methylketone that lead to carbalkoxysubstituted cyclopentanols (Eq. 2), the reaction on the contrary would start by the reduction of the enoate moiety to radical anion. Radical 4-*exo*-trig cyclisations being rather slow,[39] a competitive way would then be preferred. Protonation of the radical anion followed by one electon reduction would give the ester enolate which would finally add to the carbonyl group in a 5-*exo*-trig fashion. Interestingly, if the reaction is conducted in the absence of methanol, but only in THF with 6 equiv. of HMPA and 3 equiv. of *tert*-butanol, a 4-*exo*-trig cyclisation now takes place but with a *syn* stereoselectivity opposite to that observed with aldehydes in THF/MeOH. This switch of reactivity upon change of alcohol cosolvent has, since then, been confirmed on other related substrates by the same authors.[9f]

4. Conclusion

In the presence of SmI_2, δ-oxo-γ,γ-disubstituted-α,β-unsaturated esters readily undergo 3-*exo*-trig cyclisation. High or total diastereoselectivities in favor of the formation of '*trans*' cyclopropanol in which the OH group and the carbalkoxymethyl group are *trans* to each other are generally observed with substrates bearing a terminal aryl substituent. Total opposite stereoselectivity leading ultimately to the lactone derived from '*cis*' cyclopropanol is observed when the terminal substituent is cyclopropyl.

[‖] On the contrary, as already discussed, ring opening of **28ab** should be very fast for aryl substrates. Therefore, even if initial reduction should occur at the enoate moiety also for these substrates—for us an unlikely hypothesis—a fast equilibration between radical **28** and **18** would very likely take place rapidly. The *syn*/*anti* stereoselectivity would therefore still be related to the relative energies of the transition states leading from the radical species **28** and **18** to the dianionic species, or alternatively to the relative energies of the transition states leading from **18** to dianionic species on one hand and from **28** to **29** (lactonisation) on the other hand.



Scheme 10. [9e]

Finally when the δ-carbon bears an hydrogen atom (aldehydic substrates) or an alkyl group, a mixture of '*trans*' cyclopropanol and lactone is obtained.

'Trans' cyclopropanols are thought to arise from initial formation of ketyl radicals followed by cyclisation. On the contrary, the favored (but not necessarily exclusive) pathway to lactone would start by one electron reduction of the enoate moiety and the stereochemical issue of the reaction would be the result of samarium chelation in the cyclisation step.

5. Experimental

5.1. General information

^{1}H NMR spectra were recorded at 200 or 250 MHz and ^{13}C spectra at 63 MHz. Chemical shifts are quoted in ppm relative to TMS. High resolution mass spectra (HRMS) were obtained on a Finningan-MAT-95-S spectrometer. Infra-red spectra were taken on a Perkin-Elmer 'Spectrum One' model and in $CHCl_3$ solution.

5.2. Preparation of starting compounds

5.2.1. Preparation of β-keto-aldehydes RCOC(R′R′)-CHO with R′, R′=Me, Me or $(CH_2)_5$. For R=Ph, 2-furyl, 2-thienyl, CH_3, *c*-C_3H_7 and R′, R′=Me, Me, the β-keto-aldehydes were prepared by condensation of acyl chlorides with the morpholino-enamine of isobutyraldehyde[35] as described by Inukai and Yoshizawa.[13] The acetylation procedure was followed for acylation with aliphatic acyl chlorides and the benzoylation procedure was followed for acylation with aromatic acyl chlorides. The β-ketoaldehyde $CH_3COC(RR')CHO$ ($R'R'=(CH_2)_5$) was prepared in the same way by acetylation of the morpholino-enamine of cyclohexane carboxaldehyde according to the first procedure. *i*-$C_3H_7COC(CH_3)_3CHO$ was prepared by aldol autocondensation of isobutyraldehyde[15] followed by oxidation of the aldol product with pyridinium chlorochromate.[40] 1-naphthyl-$COC(CH_3)_2CHO$ was prepared by acylation of isobutyraldehyde pyrrolidino-enamine[41] with 1-naphthoyl chloride according to Kuhlmey et al.[14] Probably better yields would have been obtained if other β-ketoaldehydes had similarly been prepared from pyrrolidino-enamines instead of morpholino-enamines.

R′, R′=Me, Me; R=CH_3: 2,2-Dimethyl-3-oxo-butanal. Yield 66% (crude product); oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.60 (s, 1H); 2.09 (s, 3H); 1.34 (s, 6H).

R′, R′=Me, Me; R=*i*-C_3H_7: 3-Oxo-2,2,4-trimethyl-pentanal. Yield (over two steps, see above): 38%; oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.61 (s, 1H); 2.92 (sept, *J*=7 Hz, 1H); 1.32 (s, 6H); 1.04 (d, *J*=7 Hz, 6H).

R′, R′=Me, Me; R=*c*-C_3H_7: 3-Cyclopropyl-2,2-dimethyl-propanal. Purified by distillation, bp 60 °C, 5 Torr; yield 40%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.58 (s, 1H); 2.07–1.9 (m, 1H); 1.37 (s, 6H); 1.05–0.92 (m, 2H); 0.92–0.80 (m, 2H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 208.9; 201.1; 60.3; 17.7; 10.7; 7.4. IR ($CHCl_3$): 1729.5, 1692 cm^{-1}.

R′, R′=Me, Me; R=Ph: 2,2-Dimethyl-3-oxo-3-phenyl-propanal. Purified by column chromatography (AcOEt/cyclohexane 10:90); yield 50%; oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.75 (s, 1H); 7.82–7.25 (m, 5H); 1.45 (s, 6H). IR ($CHCl_3$): 1731.5, 1675.5 cm^{-1}.

R′, R′=Me, Me; R=2-furyl: 2,2-Dimethyl-3-(2-furyl)-3-oxo-propanal. Yield 66% (crude product); oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.4 (s, 1H); 7.54 (d, ^3J=1.0 Hz, 1H); 7.17 (d, ^3J=4.5 Hz, 1H); 6.49 (dd, ^3J=4.5, 2.0 Hz, 1H); 1.4 (s, 6H). IR ($CHCl_3$): 1732, 1664 cm^{-1}.

R′, R′=Me, Me; R=2-thienyl: 2,2-Dimethyl-3-oxo-3-(2-thienyl)-propanal. Yield 74% (crude product); oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.73 (s, 1H); 7.65 (d, ^3J=1.0 Hz, 1H); 7.63 (d, ^3J=5 Hz, 1H)); 7.11–7.07 (m, 1H); 1.49 (s, 6H). IR ($CHCl_3$): 1728, 1653 cm^{-1}.

R′, R′=Me, Me; R=1-naphthyl: 2,2-Dimethyl-3-(1-naphthyl)-3-oxo-propanal. Yield (crude product): 70%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.79 (s, 1H); 9.10 (d, *J*=8.5 Hz, 1H); 8.75 (d, *J*=8.5 Hz, 1H), 8.59 (d, *J*=8 Hz, 1H), 8.19–8.08, 7.96–7.84, 7.77–7.32 (three m, 3H); 1.50 (s, 6H). HRMS (EI) calcd for $C_{15}H_{14}O_2$ 226.0994, found 226.0990. IR ($CHCl_3$): 1687, 1727.5 cm^{-1}.

R′, R′=$(CH_2)_5$; R=CH_3: 1-Acetyl-cyclohexanecarboxaldehyde: Purified by column chromatography (AcOEt/cyclohexane 20:80); yield 30%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.43 (s, 1H); 2.09 (s, 3H); 2.08–1.26 (m, 10H). IR ($CHCl_3$): 1731, 1699 cm^{-1}.

R′, R′=$(CH_2)_5$; R=2-furyl: 1-(2-Furoyl)-cyclohexanecarboxaldehyde: Purified by chromatography; yield 45%. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.65 (s, 1H); 7.43 (d, J=1.5 Hz, 1H); 7.08 (d, J=3.5 Hz, 1H); 6.38 (dd, J=1.5, 3.5 Hz, 1H); 1.48–1.21 (m, 10H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 200.7; 186.5; 151.2; 146.0; 118.9; 112.1; 49.5; 28.5; 25.5; 21.8.

5.2.2. Preparation of benzyl δ-oxo-α,β-unsaturated esters 1a–g and 2a,b. **1a–g** and **2a**,**b** were prepared by Wadsworth–Emmons olefination of β-keto-aldehydes with benzyl dimethoxyphosphonoacetate.[42] The experimental procedure was the same as that used by Nicolaou and co-workers[43] for Wadsworth–Emmons olefination of 3-oxo-2,2-dimethyl-l pentanal with *tert*-butyl diethoxyphosphonoacetate. Purification of crude products was achieved by column chromatography on silica with appropriate mixtures of AcOEt and heptane or cyclohexane as the eluents.

Benzyl 4,4-dimethyl-5-oxo-5-phenyl-pent-2-enoate (**1a**). Purified by column chromatography (AcOEt/cyclohexane 10:90); yield 77%; oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.60–7.15 (m, 11H); 6 (d, ^3J=15 Hz, 1H); 5.15 (s, 2H); 1.41 (s, 6H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 202.8; 166.5; 153.8; 136.6; 136.1; 132.6; 129.5; 128.9; 128.8; 128.7; 128.6; 120.4; 66.9; 50.1; 26.3. IR ($CHCl_3$): 1717, 1681.5, 1642 cm^{-1}.

Benzyl 4,4-dimethyl-5-(2-furyl)-5-oxo-pent-2-enoate (**1b**). Purified by column chromatography (AcOEt/cyclohexane 10:90); yield 63%; white solid mp 53 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.47 (d, J=2 Hz, 1H); 7.29 (m, 6H); 7.13 (d, J=4 Hz, 1H); 6.42 (dd, J=2, 4 Hz, 1H); 5.90 (d, ^3J=16 Hz, 1H); 5.12 (s, 2H); 1.40 (s, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 189.6; 166.2; 152.0; 146.0; 135.2; 128.5; 128.3; 120.1; 119.3; 112.0; 66.1; 48.8; 24.3. IR ($CHCl_3$): 1716.5, 1669, 1645 cm^{-1}.

Benzyl 4,4-dimethyl-5-oxo-5-(2-thienyl)-pent-2-enoate (**1c**). Purified by column chromatography (AcOEt/cyclohexane 10:90); yield 80%; white solid mp: 69 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.67 (d, J=4 Hz, 1H); 7.6–7.05 (m, 8H); 6.08 (d, ^3J=16 Hz, 1H); 5.20 (s, 2H); 1.48 (s, 6H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 194.5; 167.1; 153.4; 142.4; 136.1; 133.9; 133.7; 128.9; 128.7; 128.6; 128.3; 120.7; 66.4; 49.9; 25.9. IR ($CHCl_3$): 1717; 1694 (shoulder), 1646 cm^{-1}.

Benzyl 4,4-dimethyl-5-(1-naphthyl)-5-oxo-pent-2-enoate (**1d**). Purified by column chromatography (AcOEt/cyclohexane 20:80); yield 48%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.97–7.28 (m, 13H); 6.03 (d, ^3J=16 Hz, 1H); 5.21 (s, 2H); 1.45 (s, 6H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 194.5; 167.1; 153.4; 136.1; 133.9; 133.7; 128.9; 128.7; 128.6; 128.3; 120.7; 66.4; 49.9; 25.9. HRMS (EI) calcd for $C_{24}H_{22}O_3$ 358.1569, found 358.1568. IR ($CHCl_3$): 1717, 1693.5, 1645 cm^{-1}.

Benzyl 4,4-dimethyl-5-oxo-hex-2-enoate (**1e**). Purified by column chromatography (AcOEt/cyclohexane 20:80); yield 75%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.32 (m, 5H); 7.05 (d, ^3J=16 Hz, 1H); 5.90 (d, ^3J=16 Hz; 1H); 5.14 (s, 2H); 2.07 (s, 3H); 1.23 (s, 6H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 208.8; 166.0; 135.6; 128.5; 128.3; 120.5; 66.4; 50.8; 25.9; 23.4. HRMS (EI) calcd for $C_{15}H_{18}O_3$ 246.1260, found 246.1256.

Benzyl 5-oxo-4,4,6-trimethyl-hept-2-enoate (**1f**). Purified by column chromatography (AcOEt/cyclohexane 15:85); yield 72%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.41–7.22 (m, 5H); 7.11 (d, ^3J=16 Hz, 1H); 5.94 (d, ^3J=16 Hz, 1H); 3.01 (sept, ^3J=7 Hz, 1H); 1.26 (s, 6H); 1.04 (d, ^3J=7 Hz, 6H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 215.3; 166.4; 152.1; 136.1; 128.9; 128.6; 120.9; 66.8; 51.5; 36.0; 23.6; 20.3. IR ($CHCl_3$): 1710.5, 1646 cm^{-1}.

Benzyl 5-cyclopropyl-4-4,-dimethyl-5-oxo-pent-2-enoate (**1g**). Purified by column chromatography (AcOEt/heptane 20:80); yield 65%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.43–7.12 (m, 5H); 7.16 (d, ^3J=16 Hz, 1H); 5.96 (d, ^3J=16 Hz, 1H); 5.17 (s, 2H); 2.08–1.95 (m, 1H); 1.30 (s, 6H); 1.05–0.92 (m, 2H); 0.92–0.80 (m, 2H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 210.9; 166.4; 152.6; 136.1; 128.8; 128.5; 128.4; 120.7; 66.6; 51.0; 23.7; 17.4; 12.0 HRMS (EI) calcd for $C_{17}H_{20}O_3$ 166.0993, found 166.0991; IR ($CHCl_3$) 1716.5, 1698, 1647 cm^{-1}.

Benzyl 3-[1-(2-furoyl) cyclohexyl]-prop-2-enoate (**2a**). Purified by column chromatography (AcOEt/heptane 20:80); yield 27%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.49 (d, J=1.5 Hz, 1H); 7.31 (m, 6H); 7.16 (d, J=3.5 Hz, 1H); 6.45 (dd, J=1.5, 3.5 Hz, 1H); 5.90 (d, ^3J=16 Hz, 1H); 5.14 (s, 2H); 2.17–1.41 (m, 10H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 189.3; 166.1; 156.4; 146.4; 135.7; 128.5; 128.1; 121.9; 118.8; 111.8; 65.9; 52.9; 33.4; 25.5; 22.4. HRMS (EI) calcd for $C_{21}H_{22}O_4$ 338.1518, found 338.1512.

Benzyl 3-(1-acetylcyclohexyl)-prop-2-enoate (**2b**). Purified by column chromatography (AcOEt/cyclohexane 10:90); yield 74%; white solid; mp 47 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.35 (m, 5H); 6.87 (d, ^3J=16 Hz, 1H); 5.89 (d, ^3J=16 Hz, 1H); 5.16 (s, 2H); 2.08 (s, 3H); 1.99–1.40 (m, 10H) ^{13}C NMR (63 MHz, $CDCl_3$) δ 208.5; 166.3; 151.5; 136.1; 128.9; 128.7; 122.5; 66.8; 55.7; 32.9; 26.5; 25.9; 22.9. HRMS (EI) calcd for $C_{18}H_{22}O_3$: 274.1574, found 274.1574. IR ($CHCl_3$): 1708.5, 1643 cm^{-1}.

5.2.3. Preparation of 2-(1,3-dithian-2-yl)-2-methylpropanal 5 and 1-(1,3-dithian-2-yl) cyclohexane carboxaldehyde 6. **5** and **6** were prepared by alkylation of the morpholino-enamines of isobutyraldehyde and cyclohexanecarboxaldehyde, respectively, with 2-chloro-1,3-dithiane. The procedure of Taylor and LaMattina was followed.[16]

2-(1,3-dithian-2-yl)-2-methylpropanal (**5**). Purified by vacuum distillation bp 56–57 °C, 0.1 Torr; yield 72% on a 40 mmol scale; white solid; mp: 50 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.41 (s, 1H); 4.25 (s, 1H); 3.01–2.58 (m, 4H); 2.07–1.69 (m, 2H); 1.10 (s, 6H). ^{13}C NMR (63 MHz,

$CDCl_3$) δ 202.2; 54.9; 49.9; 30.9; 25.6; 19.3. HRMS (EI) calcd for $C_8H_{14}OS_2$: 190.0485, found 190.0487.

1-(1,3-Dithian-2-yl)cyclohexanecarboxaldehyde (**6**). Purified by Kügelrohr distillation (180 °C, 0.03 Torr); yield 33% on a 20 mmole scale; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.52 (s, 1H); 4.16 (s, 1H); 3.20–2.50 (m, 4H); 2.03–1.17 (m, 12H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.9; 54.8; 52.7; 31.0; 28.6; 25.6; 24.5; 21.9. HRMS (EI) calcd for $C_{11}H_{18}OS_2$: 230.0795, found 230.0799.

5.2.4. Preparation of benzyl 4-(1,3-dithian-2-yl)-4-methylpent-2-enoate 7 and benzyl 4-[1-(1,3-dithian-2-yl)cyclohexyl]-but-2-enoate 8. Benzyl 4-(1,3-dithian-2-yl)-4-methylpent-2-enoate **7**: in a Schlenk tube and under argon atmosphere, 0.22 g (5.5 mmol) of sodium hydride 60% in oil was washed twice with dry pentane and put in suspension in 45 mL of anhydrous THF at 0 °C. To this suspension 1.42 g (5.5 mmol) of benzyl dimethylphosphonoacetate was added dropwise. After cessation of dihydrogen gas evolution a solution of 0.95 g (0.5 mmol) of 2-(1,3-dithian-2-yl)-2-methyl-propanal **5** was slowly added while the temperature was maintained near 0 °C. The reaction mixture was then refluxed for 5 h. The reaction mixture was cooled and water was first cautiously and then more rapidly added. The organic products were extracted with diethyl ether. The organic phase was dried over $MgSO_4$, filtrated and concentrated under vacuum to give 1.45 g (90% yield, oil) of crude benzyl 4-(1,3-dithian-2-yl)-4-methylpent-2-enoate which was found pure by NMR. This crude product was used as such in the following step.

Benzyl 4-(1,3-dithian-2-yl)-4-methylpent-2-enoate (**7**). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.35 (m, 5H); 7.04 (d, ^3J=14.5 Hz, 1H); 5.84 (d, ^3J=14.5 Hz, 1H); 5.14 (s, 2H); 4.05 (s, 1H); 2.86–2.75 (m, 4H); 2.07–1.76 (m, 2H); 1.23 (s, 6H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 166.2; 155.2; 135.8; 128.4; 128.0; 118.9; 66.1; 59.0; 41.5; 31.0; 25.6; 24.3; 19.3. HRMS (EI) calcd for $C_{17}H_{22}O_2S_2$: 322.1061, found 322.1063.

Benzyl 4-[1-(1,3-dithian-2-yl)-cyclohexyl]-but-2-enoate **8** was similarly prepared from 1-(1,3-dithian-2-yl)cyclohexanecarboxaldehyde **6**. In this case, the crude product was purified by column chromatography on silica (cyclohexane/AcOEt 95:5).

Benzyl 4-[1-(1,3-dithian-2-yl)-cyclohexyl]-but-2-enoate (**8**). Yield 95%; oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.33 (m, 5H); 6.96 (d, ^3J=16 Hz, 1H); 5.90 (d, ^3J=16 Hz, 1H); 5.17 (s, 2H); 4.15 (s, 1H); 2.83 (dd, J=8, 3.5 Hz, 4H); 2.03 (m, 4H); 1.77 (m, 2H); 1.50–1.28 (m, 6H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 166.2; 153.4; 135.9; 128.5; 128.2; 128.1; 121.7; 66.2; 58.3; 44.3; 33.2; 31.3; 28.95; 25.9; 25.7; 21.9. HRMS (EI) calcd for $C_{20}H_{26}O_2S_2$: 362.1374, found 362.1367.

5.2.5. Preparation of benzyl 4,4-dimethyl-5-oxo-pent-2-enoate 3 and benzyl 3-(1-formyl-cyclohexyl)-prop-2-enoate 4. Heating **7** or **8** in acetone/water in the presence of MeI and *sym*-collidine according to Redlich et al.[17] gave the corresponding aldehydes **3** or **4**.

Benzyl 4,4-dimethyl-5-oxo-pent-2-enoate **3**. Purified by column chromatography (petroleum ether/diethyl ether 80:20); yield 45%; oil. ^{1}NMR (250 MHz, $CDCl_3$) δ 9.33 (s, 1H); 7.26 (m, 5H); 6.92 (d, ^3J=14.5 Hz, 1H); 5.84 (d, ^3J=14.5 Hz, 1H); 5.09 (s, 2H); 1.18 (s, 6H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 200.7; 165.7; 149.2; 135.6; 128.5, 128.1; 121.5; 66.4; 49.1; 21.0. HRMS (EI) calcd for $C_{14}H_{16}O_3$: 232.1099, found 232.1100.

Benzyl 3-(1-formyl-cyclohexyl)-prop-2-enoate **4**. Purified by column chromatography (petroleum ether/diethyl ether 80:20); yield 74%. ^{1}HNMR (250 MHz, $CDCl_3$) δ 9.32 (s, 1H); 7.33 (m, 5H); 6.77 (d, ^3J=14.5 Hz, 1H); 5.88 d, ^3J=14.5 Hz, 1H); 5.15 (s, 2H); 1.90–1.32 (m, 10H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 200.8; 165.5; 148.4; 128.5; 128.3; 122.7; 66.4; 53.2; 30.5; 25.2; 22.0. HRMS (EI) calcd for $C_{17}H_{20}O_3$: 272.1412, found 272.1419.

5.3. SmI_2 mediated cyclisations

5.3.1. Preparation of SmI_2 solutions in THF. THF was distilled over benzophenone sodium and under an argon atmosphere. All experiments involving SmI_2 were carried out under an argon atmosphere using standard Schlenk techniques. Diiodoethane, used for preparation of SmI_2, was purified as follows: commercial 1,2 diodoethane was dissolved in diethyl ether and the ethereal solution was washed twice with aqueous sodium thiosulfate to remove any iodine. The organic phase was then dried on magnesium sulfate and then concentrated under vacuum to a small volume. The precipitated white solid was collected by filtration and dried on a vacuum line. All these operations were carried out in the dark.

0.1 M solutions of SmI_2 in THF were prepared in the following way: to 1.80 g (12 mmol) of samarium powder (from Labelcomat Company) was slowly added through a cannula and at room temperature a solution of 2.82 g of freshly purified 1,2-diiodoethane in 100 mL of THF. A blue-green coloration developed immediately and the reaction was somewhat exothermic. Once the addition was completed (after ca 20 min), the suspension was stirred for 12 h, upon which the reaction was considered as complete. The 0.1 M solutions of SmI_2 were of a deep blue color. They were kept as such in the presence of samarium powder in excess and under argon atmosphere for no more than 4 days.

5.3.2. Cyclisation reactions. General procedure: to a solution of 1 mmol of substrate to be cyclised and 4 mmol of *tert*-butanol in 5–6 mL of THF at 0 °C were added dropwise 22 mL (2.2 equiv.) of a 0.1 M solution of SmI_2 in THF. The reaction mixture was then stirred at room temperature with monitoring by TLC or IR spectroscopy on aliquots. Reaction were usually complete within 4–12 h. After quenching with dilute aqueous HCl, the products were extracted in diethyl ether. After drying ($MgSO_4$) and evaporation of ether, the residue was column chromatographied on silica with appropriate mixtures of ethyl acetate and heptane or cyclohexane as the eluents.

5.3.3. Physical and spectroscopic data for cyclisation products. All products were obtained as colorless oils.

5.3.3.1. Cyclopropanols 11a: (R′, R′=CH$_3$, CH$_3$). *R=H*: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.32 (m, 5H); 5.09 (s, 2H); 2.89 (d, ^3J=3 Hz, 1H); 2.29 (d, J=7.6 Hz, 2H); 1.13 (s, 3H); 0.93 (s, 3H); 0.91 (m, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 173.6; 128.6; 128.2; 66.3; 61.8; 32.6; 27.3; 19.6; 19.3. HRMS (EI) calcd for $C_{14}H_{18}O_3$ 234.1256, found 234.1256. IR ($CHCl_3$): 1732.5 cm^{-1}.

R=Me: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.34 (m, 5H); 5.15 (s, 2H); 2.27 (d, ^3J=8 Hz, 2H); 1.10 (s, 3H); 1.07 (s, 3H); 1.03 (t, ^3J=8 Hz, 1H); 0.88 (s, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 173.3; 135.9; 128.5; 128.1; 66.3; 59.7; 30.6; 29.2; 26.9; 21.3; 17.0; 16.5. HRMS (EI) calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1423.

R=i-Pr: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5H); 5.10 (s, 2H); 2.55–2.40 and 2.28–2.10 (two dd, *AB*X system J_{AB}=16.5 Hz, J_{AX}=6.5 Hz; J_{BX}=8.5 Hz, (1+1)H); 1.62–1.51 (m, 1H); 1.19 (s, 3H); 1.12–1.01 (m, 1H); 1.00–0.98 (m, 9H). HRMS (EI) calcd for $C_{17}H_{24}O_3$: 276.1725, found 276.1723. IR ($CHCl_3$): 1732 cm^{-1}.

R=Ph: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.4–7.15 (m, 10H); 5.12 (two d, AB system, J_{AB}=12 Hz, 2H); 2.58–2.41 and 2.18–2.05 (two dd, *AB*X system, J_{AB}=18 Hz, J_{AX}=7 Hz, J_{BX}=6.5 Hz, (1+1)H); 1.4 (s, 3H); 1.4–1.28 (m, 1H); 0.9 (s, 3H). HRMS (EI) calcd for $C_{20}H_{22}O_3$ 310.1569, found 310.1572. IR ($CHCl_3$): 1732 cm^{-1}.

R=2-furyl: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.36–7.31 (m, 6H); 6.31–6.22 (m, 2H); 5.15 (two d, AB system, J_{AB}=12 Hz, 2H); 2.61–2.51 and 2.37–2.26 (two dd, *AB*X system, J_{AB}=17.5 Hz, J_{AX}=7.5 Hz, J_{BX}=8 Hz, (1+1)H); 1.44–134 (m, 1H); 1.37 (s, 3H); 0.95 (s, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 173.1; 153.5; 142.2; 135.9; 128.6; 128.3; 127.0; 110.1; 109.1; 66.5; 59.2; 31.6; 31.2; 26.2; 21.2; 17.9. IR ($CHCl_3$): 1732.5 cm^{-1}.

R=2-thienyl: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.20 (m, 6H); 6.87–6.72 (m, 2H); 5.08 (two d, AB system, J_{AB}=12 Hz, 2H), 2.63–2.51 and 2.35–2.23 (two dd, *AB*X system, J_{AB}=17.5 Hz, J_{AX}=7 Hz, J_{BX}=8 Hz, (1+1)H); 1.34 (m, 1H); 1.32 (s, 3H); 0.92 (s, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 173.4; 142.7; 136.3; 129.0; 128.7; 128.0; 127.1; 126.6; 66.9; 60.9; 32.6; 32.1; 26.9; 21.8; 19.4. IR ($CHCl_3$): 1732.5 cm^{-1}.

R=1-naphthyl: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.1–7.7, 7.65–7.1 (two m, 12H); 5.25–5.12 (two broad d (app. q), AB system, 2H); 3.0–2.75 and 2.61–2.24 (two broad dd, *AB*X system, $J_{AB}\approx$16 Hz, $J_{BX}\approx$6 Hz; $J_{AX}\approx$8 Hz, (1+1)H); 1.59–1.39 (m, 4H); 0.65 (broad s, 3H). HRMS (EI) calcd for $C_{24}H_{24}O_3$ 360.1725, found 360.1710. IR ($CHCl_3$): 1732 cm^{-1}.

5.3.3.2. Cyclopropanols 11b: R′, R′=(CH$_2$)$_5$. *R=H*: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.30 (m, 5H), 5.11 (s, 2H); 2.98 (d, 1H, ^3J=3.0 Hz); 2.44–2.20 (two close dd, *AB*X system J_{AB}=17 Hz, J_{AX}=7.5 Hz, J_{BX}=8.0 Hz, (1+1)H); 1.65–1.23 (m, 10H); 0.88 (dt, ^3J_d=3, ^3J_t=7.5 Hz, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 166.0; 135.7; 128.5; 128.3; 128.0; 66.4; 50.8; 39.7; 25.9; 25.2; 23.4. HRMS (EI) calcd for $C_{17}H_{22}O_3$ 274.1574, found 274.1574. IR ($CHCl_3$): 1732 cm^{-1}.

R=CH$_3$: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.41–7.24 (m, 5H); 5.11 (s, 2H); 2.41–2.14 (two close dd, ABX system J_{AB}=16 Hz, J_{AX}=7.5 Hz, J_{BX}=7.5 Hz, (1+1)H); 1.65–1.15 (m, 13H); 0.91 (t, ^3J=7.5 Hz, 1H). HRMS (EI) calcd for $C_{18}H_{24}O_3$ 288.1725, found 288.1723. IR ($CHCl_3$): 1731.5 cm^{-1}.

R=2-furyl: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.36 (m, 6H); 7.30 (m, 1H); 6.23 (m, 1H); 5.12 (d, J=6 Hz, 2H); 2.60–2.47 and 2.40–2.32 (two dd, *AB*X system, J_{AB}=17 Hz, J_{AX}=7.5 Hz, J_{BX}=7.5 Hz (1+1)H); 1.80–1.12 (m, 11H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 173.1; 153.4; 142.0; 135.8; 128.5, 128.3; 127.6; 110.0; 108.7; 66.4; 59.7; 32.8; 31.5; 31.1; 31.0; 28.1; 26.3; 25.8; 25.1. HRMS (EI) calcd for $C_{21}H_{24}O_4$ 288.1725, found 288.1723. IR ($CHCl_3$): 1732 cm^{-1}.

5.3.3.3. Lactones 12a: R′, R′=CH$_3$, CH$_3$. *R=H*: ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.95 (d, ^3J=6.3 Hz, 1H); 2.78–2.67 (dd) and 2.33 (d) (*AB*X system J_{AB}=21 Hz, J_{AX}=8 Hz, J_{BX}=0 Hz, (1+1)H); 1.02 (m, 7H). HRMS calcd for $C_7H_{10}O_2$ 126.0681, found 126.0677. IR ($CHCl_3$): 1775.5 cm^{-1}.

R=Me: ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.80 (dd) and 2.11 (d) (*AB*X system J_{AB}=21.0 Hz, J_{AX}=7 Hz, J_{BX}=0 Hz, (1+1)H); 1.23–0.99 (m, 10H). HRMS (EI) calcd for $C_8H_{12}O_2$ 140.0837, found 140.0840. IR ($CHCl_3$): 1772 cm^{-1}.

R=i-Pr: ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.80–2.69 (dd) and 2.40 (d) (*AB*X system J_{AB}=19.0 Hz, J_{AX}=7.5 Hz, J_{BX}=0 Hz, (1+1)H); 1.85–1.71 (sept, ^3J=7 Hz, 1H); 1.16–0.99 (m, 13H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 178.5; 78.2; 31.4; 29.1; 25.5; 24.2; 22.4; 19.6; 18.6; 14.0; HRMS (EI) calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1148. IR ($CHCl_3$): 1771.5 cm^{-1}.

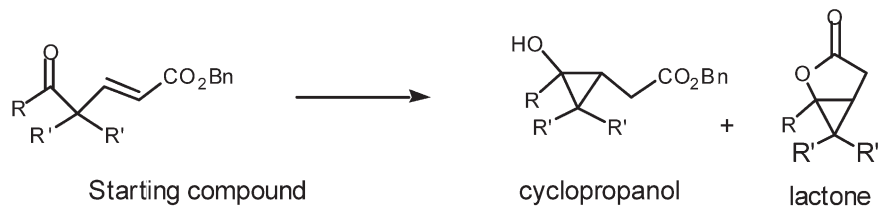
R=c-Pr: ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.76–2.58 (dd) and 2.38 (d) (*AB*X system J_{AB}=19 Hz, J_{AX}=7.0 Hz, J_{BX}=0 Hz, (1+1)H); 1.44–1.43 (m, 1H); 1.17 (s, 3H); 1.03 (s, 3H), ca 1.02 (d, partially masked, 1H); 0.77–0.55 (m, 2H); 0.48–0.23 (m, 2H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 177.9; 76.1; 31.2; 26.1; 22.5; 22.1; 13.9; 9.4; 6.0; 4.0. HRMS (EI) calcd for $C_{10}H_{14}O_2$ 166.0993, found 166.0991. IR ($CHCl_3$): 1772 cm^{-1}.

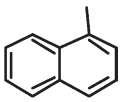
R=2-furyl: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.43–7.35 (m, 1H); 6.45–6.34 (m, 2H); 3.04–2.93 (dd) and 2.54 (d) (*AB*X system J_{AB}=19 Hz, J_{AX}=7.5 Hz, J_{BX}=0 Hz, (1+1)H); 1.78 (d, ^3J=7.5 Hz, 1H); 1.18 (s, 3H); 1.02 (s, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 177.1; 143.2; 111.2; 110.5; 67.7; 30.6; 27.5; 25.6; 22.8; 13.1. IR ($CHCl_3$): 1783 cm^{-1}.

R=2-thienyl: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.42–7.31 (m, 1H); 7.13–6.98 (m, 2H); 3.07–2.96 (dd) and 2.59 (d) (*AB*X system, J_{AB}=19 Hz, J_{AX}=7.5 Hz, J_{BX}=0 Hz, (1+1)H); 1.77 (d, ^3J=7.5 Hz, 1H); 1.17 (s, 3H); 1.02 (s, 3H). IR ($CHCl_3$): 1773 cm^{-1}.

R=1-naphthyl: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.03 (d, J=8 Hz, 1H); 7.97–7.79, 7.64–7.42 (two m, 6H); 3.25–3.0 and 2.71 (dd and d, ABX system, J_{AB}=19 Hz, J_{AX}=7 Hz, J_{BX}=0 Hz, (1+1)H); 1.92 (d, ^3J=7 Hz, 1H); 1.41 (s, 3H);

Table 1.



Entry	Starting compound				Cyclopropanol **11** (%)[a]	Lactone **12** (%)[a]	*anti*/*syn* selectivity (S)	
	R	R′R′	No.				(A)[b]	(B)[c]
1	Ph	MeMe	**1a**		85	—	100/0	95/5
2a		MeMe	**1b**	Run 1	73	13	85/15	87/13
2b				Run 2	82	14	85/15	84/16
3		$(CH_2)_5$	**2a**		77	8	91/9	88/12
4		MeMe	**1c**		60	10	86/14	85/15
5a		MeMe	**1d**	Run 1	30	49	38/62	28/72
5b				Run 2	20	47	30/70	26/74
6a	CH_3	MeMe	**1e**	Run 1	60	22	73/27	71/29
6b				Run 2	55	23	70/30	66/33
7		$(CH_2)_5$	**2b**		52	30[d]	63/37	64/66
8a	*i*-C_3H_7	MeMe	**1f**	Run 1	58	35[e]	62/38	61/39
8b				Run 2	58	30[e]	66/34	70/30
9a	*c*-C_3H_7	MeMe	**1g**	Run 1	—	92	0/100	0/100
9b				Run 2	—	95	0/100	0/100
9c				Run 3	—	90	0/100	0/100
10	H	MeMe	**3**		37	30	55/45	53/47
11a				Run 1	30	21	59/61	54/46
11b		$(CH_2)_5$	**4**	Run 2	26	32	44/66	50/50

[a] Yields of pure compounds after separation by chromatography.
[b] Calculated from *S*=yield of **11**/yield of **12**.
[c] Deduced from NMR on crude reaction mixtures by integration of benzylic H peaks of **11** and of benzylic alcohol thus assuming that all benzyl alcohol is produced by lactonisation.
[d] 10% of alcohol of direct reduction **9** was also obtained.
[e] 8–10% of saturated ester **10** was also obtained.

0.79 (s, 3H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 177.6; 134,7; 134,1; 133.7; 130.2; 128.7; 128.6; 127.2; 126.6; 125.3; 74.6; 31.4; 31.3; 15.6; 13.7. HRMS (EI) calcd for $C_{17}H_{16}O_2$ 252.1147, found 252.1150. IR ($CHCl_3$): 1776 cm^{-1}.

5.3.3.4. Lactones 12b: R′, R′=(CH$_2$)$_5$. *R=H*: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.95 (d, ^3J=6.2 Hz, 1H); 2.80–2.60 (dd) and 2.32 (d) (*AB*X system, J_{AB}=19.0 Hz, J_{AX}=7.5 Hz; J_{BX}=0 Hz, (1+1) H); 1.54–1.16 (m, 11H). HRMS (EI) calcd for $C_{10}H_{14}O_2$ 166.0994, found 166.0985. IR ($CHCl_3$): 1775.5 cm^{-1}.

R=CH$_3$: ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.87–2.76 (dd) and 2.40 (d) (*AB*X system, J_{AB}=19.0 Hz, J_{AX}=7.0 Hz; J_{BX}=0), (1+1) H); 1.79–1.15 (m, 13H); 1.06 (d, ^3J=7 Hz, 1H). HRMS (EI) calcd for $C_{11}H_{16}O_2$: 180.1150, found 180. 1147. IR ($CHCl_3$): 1770 cm^{-1}.

R=2-furyl: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.39 (m, 1H); 7.31 (m, 1H); 6.40 (m, 1H); 2.91 (dd) and 2.50 (d, *AB*X system, J_{AB}=19.0 Hz, J_{AX}=7.5 Hz, J_{BX}=0 Hz, (1+1) H); 1.72 (d, J=7.5 Hz, 1H); 1.65–1.12 (m, 10H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 178.0; 150.6; 143.1; 110.9; 110.4; 56.8; 32.6; 30.2; 26.0; 25.1; 24.7; 24.5; 23.6 (Table 1).

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