# A Radical Roundabout for an Unprecedented Tandem Reaction Including a Homolytic Substitution with a Titanium-Oxygen Bond

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**Keywords:** Epoxides / Homolytic substitution / Tetrahydrofurans / Titanium / Radical chemistry

Conceptually novel homolytic substitutions ($S_H2$) of $ClCp_2Ti$–O bonds with benzylic, secondary and tertiary alkyl radicals are described. The intermediates and crucial transition structures were studied by DFT methods. The resulting atom economical radical tandem reaction can be utilized for the synthesis of structurally complex tetrahydrofurans from simple starting materials and is therefore of interest for natural product synthesis.

## Introduction

Over the last few decades radical chemistry has been increasingly used in the synthesis of complex molecules.[1−4] This is mainly due to radical generation being possible under the mild conditions typical of chain reactions, the high predictability of carbon−carbon bond-forming reactions, and the outstanding functional-group tolerance of the transformations. However, there are also some disadvantages of free-radical chain reactions. Probably the most important drawback is the indispensable stoichiometric use of often toxic or sensitive reagents, such as stannanes or silanes,[5] in reductive reactions that usually consume two functional groups. Also, the course of the reaction can usually not be easily controlled[6−10] even though enantioselective radical processes involving chelation of radicals and radical traps with chiral Lewis acids have recently produced impressive results.[11]

An alternative approach to free-radical reactions involves electron transfer from low-valent metal complexes to suitable radical precursors.[9] This approach allows reagent control to be achieved by varying the metal and its ligands.

In this context samarium-diiodide-mediated reactions with carbonyl compounds have attracted considerable interest over the last two decades.[12−16] However, the high cost of the metal renders any large scale application unattractive. Moreover, the introduction of enantiomerically pure ligands has proven difficult and only one example of a stoichiometric enantioselective addition of a ketyl radical to an olefin, which proceeded with low selectivity, has been reported.[17] Other reagents, for example low-valent chromium[18] or vanadium[19] complexes, have, as yet, not offered better prospects.[20]

An attractive method that avoids the above-mentioned shortcomings has been developed by Nugent and RajanBabu who used epoxides,[21−24] which are readily available by a number of methods from various functional groups,[25,26] as efficient radical precursors through electron transfer from stoichiometric amounts of titanocene(III) reagents. The overall driving force of the reaction is the release of the epoxide's ring strain and the formation of the titanium−oxygen bond. Numerous interesting applications in the synthesis of complex molecules have been disclosed since the initial reports.[27,28]

We have identified reaction conditions that allow the use of more elaborate titanocene(III) complexes for reagent-controlled transformations in catalytic quantities.[29−34] In this manner the first enantioselective generation of radicals has been realized.[35−37]

In this publication we report a methodology that utilizes catalytic ring-closing reactions of radicals containing titanocene alkoxides to yield tetrahydrofurans, as shown in Figure 1.[38]

The presence of highly substituted tetrahydrofurans in many natural products should result in a broad synthetic interest in our novel method. The resulting transformation is complementary to the electron-transfer-induced ring opening of tetrahydrofurans by Lewis acid catalysis with

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Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

DOI: 10.1002/ejoc.200400001

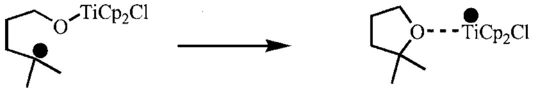


Figure 1. Formation of tetrahydrofurans by a novel radical cyclization

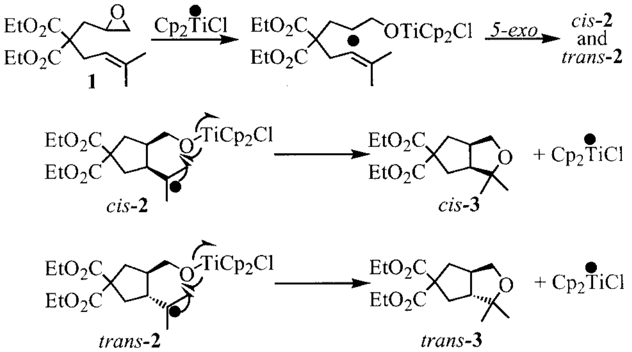
radical anions derived from arenes, as developed by Mudryk and Cohen.[39]

## Results and Discussion

### General Considerations

Our conceptually novel transformation is counterintuitive because a supposedly strong titanium–oxygen bond is cleaved to generate a tetrahydrofuran and titanocene(III) chloride. During this process titanium(IV) is reduced to titanium(III) by radical attack on a titanium–oxygen bond.

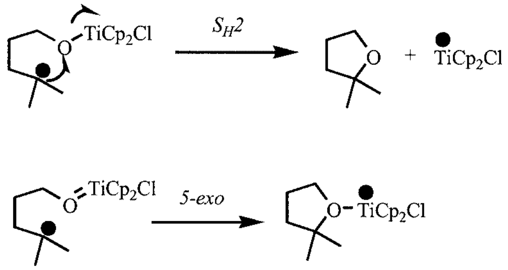
Of course, an efficient method for the generation of the necessary radicals is essential for any application in synthesis. We decided to implement a radical tandem reaction[40] that meets this requirement, as shown in Scheme 1.



Scheme 1. Radical tandem sequence for the construction of bicyclo[3.3.0] systems

The sequence is initiated by the titanocene-mediated reductive epoxide opening[21−24,29−34] of **1** and continued by a 5-*exo* cyclization onto a trisubstituted olefin to obtain the crucial radical **2**. In this intermediate the radical center is positioned appropriately for ring closure to yield the desired tetrahydrofuran.

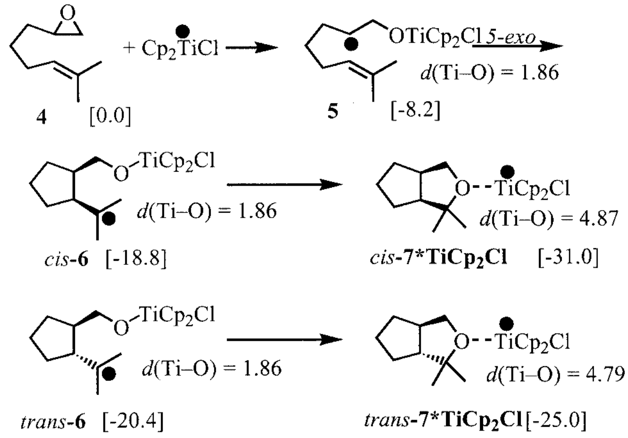
Besides the thermodynamic feasibility of the Ti–O bond rupture, two issues deserve further consideration. In the case of *trans*-**3** a highly strained and thus probably unstable bicyclo[3.3.0] system would be formed. Furthermore, it is of general interest to understand if the carbon–oxygen bond is formed via a homolytic substitution reaction ($S_H2$)[41,42] or by a process reminiscent of 5-*exo* cyclization[43] onto a titanium–oxygen double bond as depicted in Scheme 2. Nugent and RajanBabu have suggested that in the opening of epoxides a species with a formal titanium–oxygen double bond is formed.[21]



Scheme 2. Homolytic substitution pathway versus the 5-*exo* cyclization pathway

### Computational Results

In order to clarify these points and to verify the practicability of our concept we investigated the course of the overall transformation by performing density functional theory (DFT) calculations on the model system **4** using the B-P functional and a TZVP basis set,[44] as shown in Scheme 3.



Scheme 3. Intermediates in the DFT model calculation (B-P/TZVP) of the reaction of epoxide **4**. The relative energies in brackets are given in kcal·mol$^{-1}$ and refer to the separated reactants (**4** and [Cp$_2$TiCl]; bond lengths are given in Å).

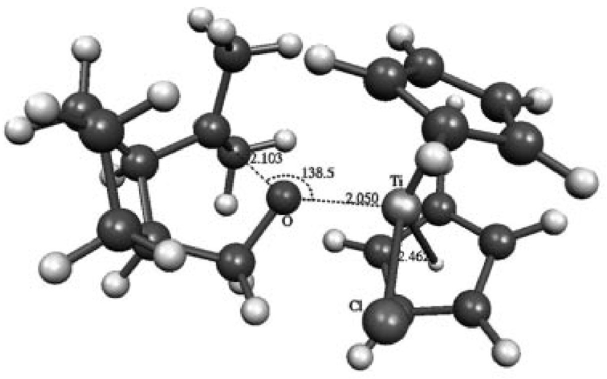
As expected both the ring opening of **4** (−8.2 kcal·mol$^{-1}$ compared to the isolated reactants) and the 5-*exo* cyclizations leading to **6** are exothermic. The calculated Ti–O bond lengths (1.86 Å) in titanocene alkoxides and enolates are in excellent agreement with values obtained from crystallographic structures (1.85 Å–1.89 Å).[48−51]

The calculations suggest that the well documented kinetically controlled course of 5-*exo* cyclizations that has been manifested in the Beckwith–Houk rules[52,53] is occurring in our case too. Thus, despite the thermodynamic preference for the formation of *trans*-**6** (−12.2 kcal·mol$^{-1}$) the other diastereoisomer *cis*-**6** (−10.6 kcal·mol$^{-1}$) is formed preferentially due to an energy of activation (6.1 kcal·mol$^{-1}$ for *cis*-**6** and 7.6 kcal·mol$^{-1}$ for *trans*-**6** relative to **5**) that is lower by 1.5 kcal·mol$^{-1}$ according to our calculations.

The tetrahydrofuran-forming reaction that yields the titanocene(III) complexes of *cis*- and *trans*-**7** were analyzed next. Both reactions were calculated to be exothermic ($-12.2$ and $-4.6$ kcal·mol$^{-1}$, respectively). A plausible reason for this finding is the high stability of the titanium-centered radical [$Cp_2TiCl$]. The lower value for *trans*-**7** reflects the strain of the *trans*-fused bicyclo[3.3.0] system and suggests that only *cis*-**3** will be preparatively accessible.

The geometries of the optimized product complexes [**7**·$Cp_2TiCl$], which are only slightly more stable than the separated molecules, show a very loose coordination between the tetrahydrofuran and titanium. The accurate determination of this complexation energy is beyond the scope of the applied DFT methods and the numbers given are also affected by basis-set-incompleteness effects. This is, however, not of much practical relevance; since entropy effects will favor the dissociation of the product complex, $\Delta G$ will most likely be negative and therefore regeneration of [$Cp_2TiCl$] will be favored. Of course, this weak coordination is beneficial for catalysis because ligand exchange with the solvent or the substrate is easy to achieve. Also, this result excludes the mechanistic possibility of the 5-*exo* type reaction shown in Scheme 2.

We have calculated the transition state for the ring closure of *cis*-**6** to *cis*-[**7**·$TiCp_2Cl$] that is shown in Figure 2.



TS-*cis*-(6-7)

Figure 2. Transition-state for the ring closure of *cis*-**6** to *cis*-[**7**·$TiCp_2Cl$] (bond lengths in Å)

The final ring closure has a relatively low barrier (+11.4 kcal·mol$^{-1}$) and should therefore be feasible even at low temperatures. The transition state exhibits similar Ti−O and C−O bond lengths. This indicates that a homolytic, concerted substitution reaction ($S_H2$) resembling the $S_N2$ reaction is taking place. However, the criteria for back-side attack seem to be less stringent for the $S_H2$ mechanism because the C−O−Ti angle is about 140° as compared to the 180° necessary for nucleophilic substitution.[54] Also the structure is fairly compact and one can expect the reaction to be sensitive to steric effects.

Qualitatively an early cyclization transition structure would be expected according to the Hammond postulate.[55] However, matters are more complicated. The electronic structure of the transition state is revealing in this context. According to the spin densities from a Mulliken population analysis, the radical center is already shifted from carbon to titanium (C +0.37, O −0.05, Ti +0.70) even though the developing C−O bond is very long (2.10 Å vs. about 1.43 Å for $Csp^3$−O). The Ti−O bond (2.05 Å) is still mostly intact. The transition structure must therefore be considered as "electronically late" although according to the bond lengths it must be regarded as early. Thus, the notion that the stability of the titanium-centered radical constitutes a major driving force for the cleavage of the Ti−O bond is already apparent in the transition structure of tetrahydrofuran formation.

The transition structure for the transformation of *trans*-**6** to *trans*-[**7**·$TiCp_2Cl$] was also calculated and a barrier of 11.7 kcal·mol$^{-1}$ was obtained for the cyclization. This value is similar to the activation energy for the formation of *cis*-[**7**·$TiCp_2Cl$], although the distance between the carbon-centered radical and oxygen is shorter (2.04 Å). Thus, the strain immanent in the *trans*-bicyclo[3.3.0] system is already partly present in the transition structure that may be considered as being "later" than the transition structure of the *cis* transformation from the viewpoint of bond-length changes.

In summary, according to the computational analysis it should be possible to realize the desired overall tandem sequence in the absence of alternative radical pathways with lower energies of activation.

## Synthetic Investigations

### *Initial Optimization*

We chose epoxy olefin **1** as the substrate for our initial examinations for two reasons. First, **1** is readily synthesized from diethyl allylmalonate by epoxidation and an $S_N2$ reaction with prenyl bromide. Secondly, it is known from the work of others[21,24] and ourselves[29,31−33] that compounds similar to **1** cyclize to yield mainly *cis*-fused radicals with selectivities of about 85:15 to 90:10.

It is also essential that competing radical pathways are excluded. The radical intermediates should therefore be relatively persistent. This is the case for **2** because tertiary radicals are trapped relatively slowly by hydrogen atom donors, for example THF, which is usually used as the solvent in titanocene-mediated or -catalyzed reactions, or a second equivalent of [$Cp_2TiCl$]. However, in the absence of other pathways this reduction, which was followed by a β-hydride elimination, has been observed.[56,57]

Our results with **1** are summarized in Table 1.

Although the emphasis of this work is on the development of catalytic conditions we initially performed the reaction in the presence of 100 mol % of [$Cp_2TiCl_2$] which was reduced either by Zn or Mn dust to obtain the crucial [$Cp_2TiCl$]. Under both conditions the desired product, *cis*-**3**, was obtained in reasonable yield (Entries 1 and 2). As expected, *trans*-**3** was neither detected nor isolated. Using Zn as the reductant longer reaction times were required to achieve conversions similar to those of Mn. Stronger com-

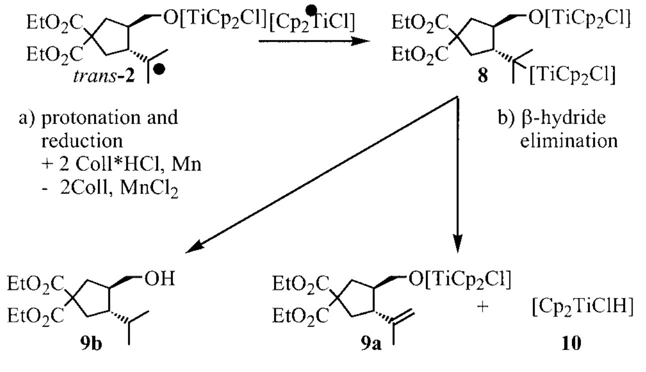
Table 1. Optimization of the transformation of **1** to *cis*-**3** at room temperature (EtOAc = ethyl acetate). All the reactions were carried out at 0.1 M concentration

| Entry | Catalyst loading [mol %] | Conditions | Yield [%] |
|---|---|---|---|
| 1 | 100 | THF, Zn (2.0 equiv.) | 50[a] |
| 2 | 100 | THF, Mn (2.0 equiv.) | 57[b] |
| 3 | 10 | Zn (2.0 equiv.) | $< 25$[c,d] |
| 4 | 10 | Mn (2.0 equiv.) | $< 20$[c,d] |
| 5 | 10 | THF, Mn (2.0 equiv.), Coll·HCl (2.5 equiv.) | 55[c] |
| 6 | 10 | THF, Zn (2.0 equiv.), Coll·HCl (2.5 equiv.) | 57[c] |
| 7 | 10 | THF, Mn (0.2 equiv.), Coll·HCl (0.5 equiv.) | 67[c] |
| 8 | 10 | THF, Mn (0.2 equiv.), Coll·HCl (0.5 equiv.) | 67[e] |
| 9 | 10 | THF, Zn (0.2 equiv.), Coll·HCl (0.5 equiv.) | 52[a] |
| 10 | 10 | EtOAc, Zn (2.0 equiv.), Coll·HCl (2.5 equiv.) | 62[a] |

[a] 24 h. [b] 16 h. [c] 20 h. [d] According to the analysis of the crude reaction mixture about 60−70% unchanged **1** was left. [e] 4 h, 70 °C.

plexation of **1** by ZnCl$_2$ than by the distinctly less Lewis acidic MnCl$_2$ retards ring opening.

The catalytic reaction conditions required some optimization. As shown in Entries 3 and 4 a simple reduction of the amount of [Cp$_2$TiCl$_2$] resulted in disappointing yields. This was also the case when the reaction was performed under higher dilution (0.01 M). The interception of *trans*-**2** by [Cp$_2$TiCl] results in the formation of the organotitanium intermediate **8** as shown in Scheme 4. Thus, two equivalents of [Cp$_2$TiCl] are consumed and complete conversion of *trans*-**2** to *trans*-**3** with 10 mol % [Cp$_2$TiCl$_2$] cannot be achieved because catalyst regeneration is prevented. Similar considerations apply to *cis*-**2**.



Scheme 4. Regeneration of [Cp$_2$TiCl] from undesired side-products

The organometallic compound **8** should decompose via β-hydride elimination to olefin **9a** and the hydrido titanium species **10** in the absence of acid. Thus the catalytic cycle is interrupted due to the consumption of [Cp$_2$TiCl].

In the presence of Coll·HCl (Coll = collidine), protonation of the Ti−O and Ti−H bonds in **9a** and **10** liberates [Cp$_2$TiCl$_2$]. Regeneration of [Cp$_2$TiCl] is accomplished by the reduction of [Cp$_2$TiCl$_2$] by the metal powder.

In addition, the double protonation of **8** to yield **9b** is also possible. In this case the [Cp$_2$TiCl$_2$] formed also needs to be reduced to regenerate the redox catalyst. Thus, two equiv. of Coll·HCl and one equiv. of the reductant are needed to regenerate [Cp$_2$TiCl] in this competing side-reaction. Similar considerations apply to *cis*-**2** in cases where THF formation is relatively slow. In all the cases examined except Entries 3 and 4 mixtures of *cis*- and *trans*-**9a** and -**9b** were obtained as side-products which accounted for 30−35% of the consumed starting material. The exact ratios of the isomers could not be determined. In Entries 3 and 4 the main product (60−70%) was the reisolated starting material.

When the reaction was run under conditions typical of reductive epoxide opening[29,31] yields of 55−57% were obtained depending on the reductant employed (Entries 5 and 6). As expected, two equivalents of the reductant and 2.5 equivalents of Coll·HCl are not needed for complete consumption of the starting material. With 0.2 equiv. of metal powder and 0.5 equiv. of the acid the best results were obtained with Mn in THF (Entry 7). Heating of the reaction mixture resulted in a faster transformation without a reduction in yield (Entry 8). In the case of Zn, EtOAc, turned out to be superior to THF as solvent (Entries 9 and 10).

We suggest that the superiority of Mn to Zn and of EtOAc, to THF in the case of Zn is due to a slower reduction of [Cp$_2$TiCl$_2$] to [Cp$_2$TiCl] (Zn: ca. 1 min in THF, 30−60 min in EtOAc; Mn: 3−5 min in THF, > 60 min in EtOAc) that can be observed by a color change from red to green. A lower concentration of the reductant will decrease the rate of the undesired bimolecular reaction of *cis*-**2** and *trans*-**2** and therefore increase the yield of *cis*-**3** (Scheme 4). A similar retardation of the bimolecular trapping can be achieved by performing the reactions under higher dilution (vide infra).

We also investigated the potential of three other complexes as catalysts for the preparation of *cis*-**3** from **1**. The results are summarized in Table 2.

While [(MeCp)$_2$TiCl$_2$] performed reasonably well (Entry 2) the bulky [(*t*BuCp)$_2$TiCl$_2$] gave a disappointing yield (Entry 3). The compact transition structure (Figure 2) supports the assumption that the system should be very sensitive towards steric interactions. Interestingly, with [CpTiCl$_3$] the desired product **3** was also obtained, although in modest yield (Entry 4). The reduced yield can be rationalized by

Table 2. Comparison of different catalysts in the preparation of **3**

| Entry | Catalyst | Conditions | Yield [%] |
|---|---|---|---|
| 1 | [$Cp_2TiCl_2$][a] | THF, Mn (2.0 equiv.), Coll·HCl (2.5 equiv.) | 55 |
| 2 | [$(MeCp)_2TiCl_2$][a] (**11**) | THF, Mn (2.0 equiv.), Coll·HCl (2.5 equiv.) | 46 |
| 3 | [$(t\text{Bu}Cp)_2TiCl_2$][a] (**12**) | THF, Mn (2.0 equiv.), Coll·HCl (2.5 equiv.) | 20 |
| 4 | [$CpTiCl_3$][b] (**13**) | THF, Mn (0.2 equiv.), Coll·HCl (0.5 equiv.) | 48 |

[a] 10 mol %. [b] 15 mol %.

the better reducing ability of the titanium(III) reagent due to the presence of only one bulky Cp ligand and a higher Ti−O bond strength.

### *Scope and Limitation of the Tetrahydrofuran-Forming Reaction*

Our method is attractive from a synthetic point of view as the molecular complexity of simple starting materials is substantially increased in a single step.[58,59] Therefore, we decided to investigate the influence of the olefin substitution pattern on the outcome of the reaction.

### Trisubstituted Olefins

As summarized in Table 3 a number of trisubstituted olefins can act as suitable radical precursors.

As shown in Entries 1 to 3 the synthesis of spirotricyclic compounds **15**, **17**, and **19** is readily achieved in yields similar to those of **3**. However, in the case of **15** and **19** the dilution technique (Zn, [EtOAc] = 0.01 M to 0.02 M) had to be applied to achieve these results. To the best of our knowledge no simple method for the synthesis of these complex products is available.

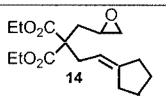
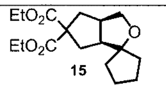
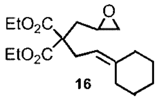
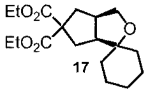
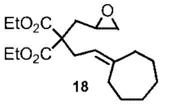
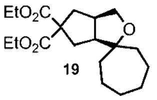
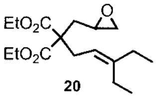
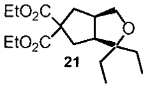
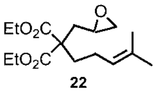
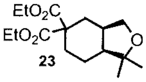
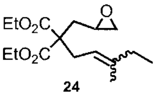
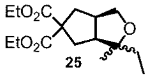
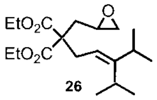
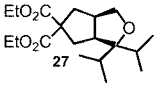
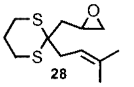
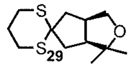
The diethyl-substituted olefin **20** (Entry 4) also readily gave the desired product **21**. The bicyclo[4.3.0] system **23** (Entry 5) demonstrates the usefulness of our titanocene catalyzed protocol. Usually 6-*exo* cyclizations are distinctly less efficient than the corresponding 5-*exo* cyclizations in contrast to our system.[1][60]

In the case of the *diisopropyl-substituted* olefin **26** (Entry 7) none of the desired product **27** was obtained. The same holds true for *tert*-butyl-substituted olefins (not shown). The approach of the intermediate radicals towards the Ti−O bond is too hindered to enable an $S_H2$ reaction.

The presence of the 1,3-dithiane unit in **28** leads to a yield and diastereoselectivity similar to those of the malonate scaffold (Entry 8). The masked ketone increases the usefulness of our method as a readily accessible additional functional group is incorporated into the reaction product **29**.

With substrate **24** [(*E*)/(*Z*) = 74:26; Entry 6] **25** was obtained as a 64:36 mixture of diastereoisomers irrespective of the reaction temperature. At −20 °C reduction of [$Cp_2TiCl_2$] became rather slow and thus 39% of the starting material was reisolated. The low diastereoselectivity reflects the geometrically early transition structure.

Table 3. Trisubstituted olefins as substrates in the THF formation.

| Entry | Substrate | Product | Yield/[%] |
|---|---|---|---|
| 1 |  **14** |  **15** | 61[a] |
| 2 |  **16** |  **17** | 62[b] |
| 3 |  **18** |  **19** | 62[c] |
| 4 |  **20** |  **21** | 64[d] |
| 5 |  **22** |  **23** | 62[e], *dr* = 87:13 |
| 6 |  **24** |  **25** | 63[d,f], *dr* = 64:36 |
| 7 |  **26** |  **27** | 0[d] |
| 8 |  **28** |  **29** | 65[g] |

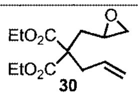
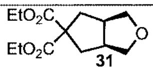
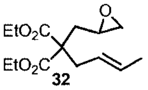
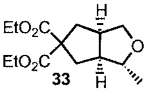
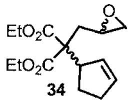
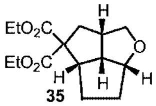
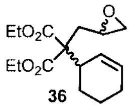
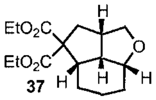
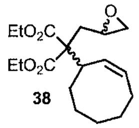
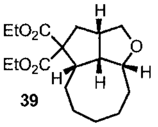
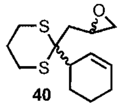
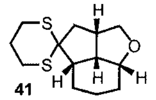
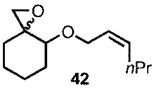
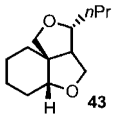
[a] 20 mol % [$Cp_2TiCl_2$], Zn (4.0 equiv.), Coll·HCl (5.0 equiv.), EtOAc (0.01 M). [b] 10 mol % [$Cp_2TiCl_2$], Mn (0.5 equiv.), Coll·HCl (2.5 equiv.), THF (0.1 M). [c] 10 mol % [$Cp_2TiCl_2$], Zn (2.0 equiv.), Coll·HCl (2.5 equiv.), EtOAc (0.02 M). [d] 10 mol % [$Cp_2TiCl_2$], Mn (2.0 equiv.), Coll·HCl (2.5 equiv.), THF (0.1 M). [e] 10 mol % [$Cp_2TiCl_2$], Mn (0.2 equiv.), Coll·HCl (0.5 equiv.), THF (0.1 M). [f] *dr* (**24**) = 74:26; 0 °C: 65%, *dr* = 63:37; −20 °C: 39%, *dr* = 63:37. [g] 20 mol % [$Cp_2TiCl_2$], Zn (2.0 equiv.), Coll·HCl (2.5 equiv.), EtOAc (0.02 M).

The reaction conditions used generally relied on the slow regeneration of [$Cp_2TiCl$] in EtOAc, as solvent at a relatively low concentration of the starting material (0.02 M) in the presence of 20 mol % [$Cp_2TiCl_2$], 2.0 equiv. of Zn, and 2.5 equiv. of Coll·HCl. In many cases the amounts of the reagents used could be substantially reduced (10 mol % [$Cp_2TiCl_2$], 0.2 equiv. of metal powder, and 0.5 equiv. of Coll·HCl), however.

### Mono- and Disubstituted Olefins

The formation of THF derivatives through the $S_H2$ reaction of mono- and disubstituted olefins was also investigated to define the overall scope of the transformation. Some of our results are summarized in Table 4.

Table 4. Mono- and disubstituted olefins as substrates in the THF formation

| Entry | Substrate | Product | Yield/[%] |
|---|---|---|---|
| 1 |  **30** |  **31** | 5[a] |
| 2 |  **32** |  **33** | 62[b], *dr* = 80:20 |
| 3 |  **34** |  **35** | 60[b] |
| 4 |  **36** |  **37** | 63[b] |
| 5 |  **38** |  **39** | 73[b] |
| 6 |  **40** |  **41** | 51[b] |
| 7 |  **42** |  **43** | 50[a,c], *dr* = 95:5 |

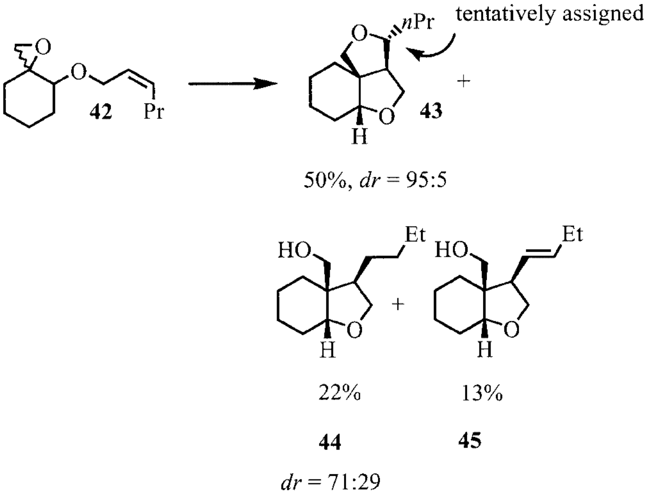
[a] 10 mol % [$Cp_2TiCl_2$], Zn (2 equiv.), Coll·HCl (2.5 equiv.), THF (0.1 M). [b] 20 mol % [$Cp_2TiCl_2$], Zn (2 equiv.), Coll·HCl (2.5 equiv.), EtOAc (0.02 M). [c] *dr* (**42**) = 88:12.

Not surprisingly, the monosubstituted alkene **30** essentially gave none of the desired **31** (5%). It is well-known that the primary radicals produced during 5-*exo* cyclization are rapidly trapped by [$Cp_2TiCl$] to yield the products of a reductive cyclization.[21–24,29–34]

Epoxides containing disubstituted olefins are good substrates for the transformation. In the case of **32**, **33** was produced with a diastereoselectivity of 80:20 in favor of the isomer shown. With cyclic olefins **34**, **36**, **38**, and **40** (Entries 3–6), which were employed as roughly 50:50 mixtures of diastereoisomers, the tricyclic products **35**, **37**, **39** and **41** were obtained as single isomers. In all cases the structural assignments are based on the relevant $^1H-^1H$ coupling constants.

Thus, the sole remaining stereocenter after epoxide opening controls the formation of three other stereocenters. Note that the synthesis of enantiomerically pure substrates by palladium-catalyzed allylic alkylation[61] is possible and offers access to products in an enantiomerically pure form. This possibility and the diastereoconvergent course of our reaction is extremely attractive for the synthesis of complex molecules.

The synthesis of **43** (Entry 7, owing to extensive overlap in the $^1H$ NMR spectrum, the structure has been tentatively assigned based on the results of modeling studies) from **42** is of interest for two reasons. Synthetically, a structurally very complex molecule is accessible in a single step from a simple precursor. From a mechanistic point of view the reaction has proved very valuable because all by-products could be isolated and characterized. These products are shown in Scheme 5.



Scheme 5. By-products of the reaction of **42**

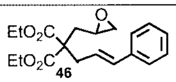
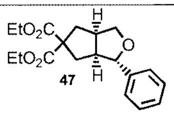
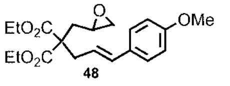
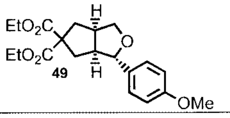
The by-products originate from the initial 5-*exo* cyclization and constitute the product of the usual reductive cyclization and protonation of the Ti–O and Ti–C bonds **44** (*dr* = 71:29) and the product **45** (single isomer) of β-hydride elimination from an organotitanium intermediate in a ratio of 63:37 in a combined yield of 35%.[33] The major isomer of **44** was assigned as *all-cis* in analogy to related systems that reacted with essentially the same selectivity.[33] The mixture of these compounds can be converted into **44** quantitatively by hydrogenation over Pd/C. It turned out that **45** was converted into the major isomer of **44**. Therefore the structure of **45** was also assigned as *all-cis.*

These findings imply that in the case of secondary radicals the trapping with a second equivalent of [$Cp_2TiCl$] can compete with tetrahydrofuran formation and that β-hydride elimination can compete kinetically with the protonation of Ti–C bonds under our protic conditions.[29–34] It remains to be seen how the reaction can be completely driven towards the tricyclic system **43** by variation of the catalyst's ligands.

### Styrenes

We also decided to investigate the role of styrenes as radical acceptors for the generation of benzylic radicals under our conditions. The resulting products — aryl-substituted tetrahydrofurans — are ubiquitous in nature, for example in the furanolignans.[62] Our results are summarized in Table 5.

Table 5. Styrenes as substrates in the THF formation

| Entry | Substrate | Product | Yield/[%] |
|---|---|---|---|
| 1 |  46 |  47 | 10[a] |
| 2 |  48 |  49 | 52[b] |

[a] 10 mol % $[Cp_2TiCl_2]$, Mn (2 equiv.), Coll·HCl (2.5 equiv.), THF (0.1 M), reflux 17%. [b] 20 mol % $[Cp_2TiCl_2]$, Zn (2 equiv.), Coll·HCl (2.5 equiv.), EtOAc (0.1 M).

While the phenyl-substituted olefin **46** gives a low yield of the desired product **47** (10%, heating resulted in a slight increase to 17%, Entry 1), the methoxy-substituted olefin **48** resulted in a much better yield of the product **49** (52%, Entry 2), which was contaminated with a trace impurity (< 3%) according to the $^1H$ NMR spectrum. It should be noted that **49** is somewhat acid labile. The reduced yield of **47** can be rationalized by the increased stability of the benzylic radical compared with *tert*-alkyl radicals (ca. 10 kcal·mol$^{-1}$) which prevents attack at the Ti−O bond. Instead the radical is reduced by a second equiv. of $[Cp_2TiCl]$.[31] In the case of **48** this reduction is retarded due to the +M-substituent and thus the product **49** was obtained in a much higher yield. Thus, the stability of the benzylic radical formed seems to be less important than its persistence towards reduction to the benzylic anion.

Very recently, Trost et al. noted a similar rearrangement in their synthesis of (−)-siccanin which produced an aryl-substituted THF in about 20% yield.[63]

## Conclusion

In summary, we have described a novel titanocene(III)-catalyzed radical tandem reaction that features the unprecedented cleavage of a titanium−oxygen bond via homolytic substitution to yield highly substituted tetrahydrofurans with high stereoselectivity. The mechanisms of all the steps have been investigated by DFT calculations that have also led to a detailed understanding of the transition structures. In the crucial step the redox active catalyst $[Cp_2TiCl]$ is regenerated. The overall reaction constitutes a rare example of an atom economical radical transformation.[64] Further work is in progress to apply this method to the synthesis of natural products, e.g. furanolignans, and to increase the efficiency of the process by catalyst tuning.

## Experimental Section

**General Remarks:** All reactions were performed in oven-dried (100 °C) glassware under $N_2$ or Ar. THF was freshly distilled from K. $Et_2O$ was freshly distilled from Na/K. Products were purified by flash chromatography[65] on Macherey−Nagel silica gel 60 and Merck silica gel 50 (eluents are given in brackets: CH refers to cyclohexane, EtOAc to ethyl acetate, $Et_2O$ to diethyl ether, MTBE to *tert*-butyl methyl ether, and PE to petroleum ether, 30−60 °C fractions). Yields refer to analytically pure samples. Isomer ratios were determined from suitable $^1H$ NMR integrals of cleanly separated signals. NMR: Bruker AMX 300, AM 400, DRX 500, Varian XR 200, and MERCURY 300 HFCP. $^1H$ NMR: [$d_5$]benzene ($\delta$ = 7.16 ppm) and $CHCl_3$ ($\delta$ = 7.26 ppm) were used as internal standards in the same solvent. $^{13}C$ NMR: $CDCl_3$ ($\delta$ = 77.16 ppm) and [$D_6$]benzene ($\delta$ = 128.06 ppm) were used as internal standards in the same solvent; integrals are in agreement with assignments, coupling constants are given in Hz and always constitute $J_{H,H}$ coupling constants. IR spectra: Perkin−Elmer 1600 series FT-IR, PARAGON 1000, and 1620; spectra were recorded as KBr pellets or as neat films on NaCl and KBr plates. Collidine hydrochloride was dried prior to use by gentle heating under vacuum.

**General Procedure 1 (GP 1):** Diethyl 2-(oxiranyl)methylmalonate (13.9 mmol) was added to a suspension of NaH [455 mg (95%), 18.0 mmol, 1.30 equiv.] and allylic bromide (16.6 mmol, 1.20 equiv.) in dry THF (75 mL) at 0 °C and the reaction mixture was stirred for 4 h at this temperature. The reaction was quenched by the addition of water (40 mL) and the aqueous layer was separated and extracted with MTBE (3 × 20 mL). The combined organic layers were washed with water (3 × 20 mL) and satd. aq. NaCl (20 mL) and dried with $MgSO_4$. After evaporation of the solvent the residue was purified by $SiO_2$ flash chromatography.

**General Procedure 2 (GP 2):** $[Cp_2TiCl_2]$ (0.10−1.00 equiv.) and Zn or Mn powder (0.20−2.00 equiv.) were added to a suspension of collidine hydrochloride (0.50−2.50 equiv.) in dry THF or ethyl acetate (10−50 mL) and the mixture stirred until the color of the suspension turned from red to green. Then the epoxide (0.50−2.00 mmol) was added and the reaction mixture was stirred overnight at room temperature. After addition of MTBE (30 mL) the suspension was filtered and the organic layer was washed with water (30 mL). The aqueous layer was separated and reextracted with $CH_2Cl_2$ (2 × 20 mL). The combined organic layers were washed with HCl (20 mL, 2 N), satd. aq. $NaHCO_3$ (20 mL), water (20 mL) and satd. aq. NaCl (20 mL) and dried with $MgSO_4$. After evaporation of the solvent the residue was purified by $SiO_2$ flash chromatography.

**Diethyl 2,2-Dimethyl-3-oxabicyclo[3.3.0]octane-7,7-dicarboxylate (3):**[20] Table 1, Entry 1: According to GP 2: $[Cp_2TiCl_2]$ (249 mg, 1.00 mmol, 1.00 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react at room temperature for 24 h. After silica gel chromatography (CyH/EtOAc, 92:8) **3** (141 mg, 50%) was isolated as a colorless liquid.

Table 1, Entry 2: According to GP 2: $[Cp_2TiCl_2]$ (249 mg, 1.00 mmol, 1.00 equiv.), Mn (110 mg, 2.00 mmol, 2.00 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react at room temperature for 16 h. Silica gel chromatography yielded **3** (162 mg, 57%) as a slightly yellow liquid.

Table 1, Entry 3: According to GP 2: $[Cp_2TiCl_2]$ (12.5 mg, 0.05 mmol, 0.10 equiv.), Zn (65.4 mg, 1.00 mmol, 2.00 equiv.) and **1** (142 mg, 0.50 mmol) in dry THF (10 mL) were allowed to react at room temperature for 20 h. NMR analysis of the crude product revealed that less then 25% of **3** was formed.

Table 1, Entry 4: According to GP 2: $[Cp_2TiCl_2]$ (12.5 mg, 0.05 mmol, 0.10 equiv.), Mn (54.9 mg, 1.00 mmol, 2.00 equiv.) and

**1** (142 mg, 0.50 mmol) in dry THF (10 mL) were allowed to react at room temperature for 20 h . NMR analysis of the crude product revealed that less then 20% of **3** was formed.

Table 1, Entry 5: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Mn (110 mg, 2.00 mmol, 2.00 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react at room temperature for 20 h. Silica gel chromatography yielded **3** (159 mg, 55%) as a colorless liquid.

Table 1, Entry 6: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react for 20 h at room temperature. Silica gel chromatography yielded **3** (164 mg, 57%) as a colorless liquid.

Table 1, Entry 7: According to GP 2: Collidine hydrochloride (79.0 mg, 0.50 mmol, 0.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mol, 0.10 equiv.), Mn (11.0 mg, 0.20 mmol, 0.20 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react at room temperature for 20 h. After silica gel chromatography **3** (190 mg, 67%) was isolated as a colorless liquid.

Table 1, Entry 8: According to GP 2: Collidine hydrochloride (79.0 mg, 0.50 mmol, 0.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mol, 0.10 equiv.), Mn (11.0 mg, 0.20 mmol, 0.20 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react at 70 °C for 4 h. After silica gel chromatography **3** (189 mg, 67%) was isolated as a colorless liquid.

Table 1, Entry 9: According to GP 2: Collidine hydrochloride (79.0 mg, 0.50 mmol, 0.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Zn (13.1 mg, 0.20 mmol, 0.20 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react for 24 h at room temperature. After silica gel chromatography **3** (148 mg, 52%) was isolated as a colorless liquid.

Table 1, Entry 10: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **1** (284 mg, 1.00 mmol) in dry ethyl acetate (10 mL) were allowed to react at room temperature for 24 h. After silica gel chromatography **3** (177 mg, 62%) was isolated as a colorless liquid.

Table 2, Entry 2: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$(MeCp)_2TiCl_2$] (27.7 mg, 0.10 mmol, 0.10 equiv.), Mn (110 mg, 2.00 mmol, 2.00 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react at room temperature for 16 h. After silica gel chromatography **3** (131 mg, 46%) was obtained as a slightly yellow liquid.

Table 2, Entry 3: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$(t\mathrm{Bu}Cp)_2TiCl_2$] (36.1 mg, 0.10 mmol, 0.10 equiv.), Mn (110 mg, 2.00 mmol, 2.00 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react at room temperature for 16 h. After silica gel chromatography **3** (57.8 mg, 20%) was obtained as a slightly yellow liquid.

Table 2, Entry 4: According to GP 2: Collidine hydrochloride (79.0 mg, 0.50 mmol, 0.50 equiv.), $CpTiCl_3$ (32.9 mg, 0.15 mmol, 0.15 equiv.), Mn (11.0 mg, 0.20 mmol, 0.20 equiv.) and **1** (284 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react at room temperature for 16 h. After silica gel chromatography **3** (136 mg, 48%) was isolated as a colorless liquid.

**Diethyl 2-(2-Cyclopentylideneethyl)-2-(oxiranyl)methylmalonate (14):** Table 3, **Entry 1:** According to GP 1: NaH [404 mg (95%), 16.0 mmol, 1.45 equiv.], diethyl 2-(oxiranyl)methylmalonate (2.81 g, 13.0 mmol, 1.15 equiv.) and (2-bromoethylidene)cyclopentane[66] (2.00 g, 11.4 mmol) were allowed to react in dry THF (50 mL) at 0 °C. While warming to room temperature, the reaction mixture was stirred for 2 h. After silica gel chromatography (CyH/EtOAc, 92:8) combined with bulb-to-bulb distillation (230 °C, 1.7 mbar) **14** (2.21 g, 64%) was isolated as a colorless solid. $R_f$ (CyH/EtOAc, 89:11) = 0.26; m.p. 47−49 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 5.08 (t, pseudo-quint, $^3J = 7.3$, $^4J = 2.4$ Hz, 1 H), AB-signal ($\delta_{A1}$ = 4.19, $\delta_{B1}$ = 4.15, $J_{AB}$ = 10.6 Hz, additionally split by $^3J = 7.1$ Hz, 2 H), 4.18 (q, $^3J = 7.1$ Hz, 2 H), 2.96 (dddd, $^3J = 6.5$, $^3J = 5.2$, $^3J = 3.9$, $^3J = 2.7$ Hz, 1 H), 2.67−2.71 (m, 3 H), 2.40 (dd, $^2J$ = 5.1, $^3J = 2.7$ Hz, 1 H), 2.14−2.22 (m, 4 H), AB-signal ($\delta_{A2}$ = 2.09, $\delta_{B2}$ = 2.02, $J_{AB}$ = 14.6 Hz, additionally split by $^3J_{(A2)}$ = 5.2 Hz and $^3J_{(B2)}$ = 6.5 Hz, 2 H), 1.51−1.68 (m, 4 H), 1.24 (t, $^3J = 7.1$ Hz, 3 H), 1.24 (t, $^3J = 7.1$ Hz, 3 H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 171.3, 171.2, 147.8, 113.1, 61.5, 61.4, 56.6, 48.8, 47.0, 36.2, 33.9 (2 C), 29.0, 26.4, 26.3, 14.1 (2 C) ppm. IR (film): $\tilde{\nu}$ = 2945, 1725, 1445, 1420, 1365, 1300, 1200, 1150, 1095, 1035, 930, 860, 770 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{17}H_{26}O_5^{+\cdot}$: 310.1780; found 310.1781 [$M^{+\cdot}$]. $C_{17}H_{26}O_5$ (310.4): calcd. C 65.78, H 8.44; found C 65.58, H 8.32.

**Diethyl Spiro[cyclopentane-1,2′-(3′-oxabicyclo[3.3.0]octane)]-7′,7′-dicarboxylate (15):** Table 3, Entry 1: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 5.00 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mmol, 0.20 equiv.), Zn (131 mg, 2.00 mmol, 4.00 equiv.) and **14** (155 mg, 0.50 mmol) in dry ethyl acetate (50 mL) were allowed to react for 60 h at room temperature. After silica gel chromatography (CyH/EtOAc, 90:10) **15** (94.4 mg, 61%) was obtained as a colorless liquid. $R_f$ (CyH/EtOAc, 89:11) = 0.22. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = AB-signal ($\delta_{A1}$ = 4.19, $\delta_{B1}$ = 4.16 ppm, $J_{AB}$ = 10.8 Hz, additionally split by $^3J = 7.1$ Hz, 2 H), 4.17 (q, $^3J = 7.1$ Hz, 2 H), AB-signal ($\delta_{A2}$ = 3.75, $\delta_{B2}$ = 3.53, $J_{AB}$ = 9.2 Hz, additionally split by $^3J_{(A2)}$ = 7.5 Hz and $^3J_{(B2)}$ = 2.8 Hz, 2 H), 2.79 (ddddd, $^3J \approx 9.0$, $^3J \approx 8.6$, $^3J = 7.6$, $^3J = 7.5$, $^3J$ = 2.8 Hz, 1 H), 2.61 (ddd, $^2J = 13.2$, $^3J \approx 8.6$, $^4J = 2.1$ Hz, 1 H), 2.50 (ddd, $^3J = 10.6$, $^3J \approx 9.0$, $^3J = 7.7$ Hz, 1 H), 2.36 (ddd, $^2J$ = 12.8, $^3J = 7.7$, $^4J = 2.1$ Hz, 1 H), 1.96 (dd, $^2J = 12.8$, $^3J = 10.6$ Hz, 1 H), 1.89 (dd, $^2J = 13.2$, $^3J = 7.6$ Hz, 1 H), 1.29−1.81 (m, 8 H), 1.23 (t, $^3J = 7.1$ Hz, 3 H), 1.23 (t, $^3J = 7.1$ Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 172.0, 171.3, 93.3, 71.5, 63.0, 61.5, 61.4, 51.4, 43.3, 40.8, 37.3, 36.8, 34.1, 24.1, 23.7, 14.2 (2 C) ppm. IR (film): $\tilde{\nu}$ = 2955, 2870, 1730, 1445, 1365, 1255, 1100, 1070, 1035, 860 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{17}H_{26}O_5^{+\cdot}$: 310.1780; found 310.1779 [$M^{+\cdot}$]. $C_{17}H_{26}O_5$ (310.4): calcd. C 65.78, H 8.44; found C 65.53, H 8.39.

**Diethyl 2-(2-Cyclohexylideneethyl)-2-(oxiranyl)methylmalonate (16): Table** 3, Entry 2: According to GP 1: NaH [253 mg (95%), 10.0 mmol, 1.25 equiv.], diethyl 2-(oxiranyl)methylmalonate (1.73 g, 8.00 mmol) and (2-bromoethylidene)cyclohexane[67] (1.51 g, 8.00 mmol, 1.00 equiv.) were allowed to react in dry THF (40 mL) for 2 h at 0 °C. After silica gel chromatography (CyH/EtOAc, 94:6) **16** (1.70 g, 65%) was obtained as a colorless oil. $R_f$ (CyH/EtOAc, 89:11) = 0.32. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 4.90 (t, pseudo-quint, $^3J \approx 7.9$, $^4J = 1.4$ Hz, 1 H), 4.11−4.24 (m, 2 H), 4.18 (q, $^3J = 7.1$ Hz, 2 H), 2.95 (dddd, $^3J = 6.6$, $^3J = 5.2$, $^3J = 3.9$, $^3J = 2.7$ Hz, 1 H), AB-signal ($\delta_{A1}$ = 2.74, $\delta_{B1}$ = 2.70, $J_{AB}$ = 14.7 Hz, additionally split by $^3J \approx 7.9$ Hz, 2 H), 2.70 (dd, $^2J = 5.2$, $^3J = 3.9$ Hz, 1 H), 2.40 (dd, $^2J = 5.2$, $^3J = 2.7$ Hz, 1 H), 2.01−2.17 (m, 4 H), AB-signal ($\delta_{A2}$ = 2.09, $\delta_{B2}$ = 2.00, $J_{AB}$ =

14.5 Hz, additionally split by $^{3}J_{(A2)} = 5.2$ Hz and $^{3}J_{(B2)} = 6.6$ Hz, 2 H), 1.43−1.55 (m, 6 H), 1.24 (t, $^{3}J = 7.1$ Hz, 3 H), 1.24 (t, $^{3}J = 7.1$ Hz, 3 H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 171.2 (2 C), 144.1, 114.3, 61.5, 61.4, 56.6, 48.7, 47.0, 37.6, 36.0, 31.3, 29.0, 28.7, 27.9, 26.9 14.1 (2 C) ppm. IR (film): $\tilde{\nu}$ = 2930, 2855, 1730, 1445, 1365, 1285, 1220, 1095, 1035, 935, 860 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{18}H_{28}O_5^{+\cdot}$: 324.1937; found 324.1941 [M$^{+\cdot}$]. $C_{18}H_{28}O_5$ (324.4): calcd. C 66.64, H 8.70; found C 66.82, H 8.91.

**Diethyl Spiro[cyclohexane-1,2′-(3′-oxabicyclo[3.3.0]octane)]-7′,7′-dicarboxylate (17):** Table 3, Entry 2: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv. [Cp$_2$TiCl$_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Mn (27.0 mg, 0.50 mmol, 0.50 equiv.) and **16** (324 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react for 60 h at room temperature. After silica gel chromatography (CyH/EtOAc, 85:15) **17** (203 mg, 62%) was obtained as a colorless liquid. $R_f$ (CyH/EtOAc, 89:11) = 0.32. $^{1}$H NMR (300 MHz, CDCl$_3$): δ = 4.18 (q, $^{3}J = 7.1$ Hz, 2 H), 4.15 (q, $^{3}J = 7.1$ Hz, 2 H), 3.88 (dd, $^{2}J \approx 9.1$, $^{3}J \approx 7.8$ Hz, 1 H), 3.53 (dd, $^{2}J \approx 9.1$, $^{3}J = 3.4$ Hz, 1 H), 2.85 (ddddd, $^{3}J \approx 8.8$, $^{3}J = 8.5$, $^{3}J \approx 7.8$, $^{3}J \approx 7.6$, $^{3}J = 3.4$ Hz, 1 H), 2.61 (ddd, $^{2}J = 13.2$, $^{3}J = 8.5$, $^{4}J = 2.1$ Hz, 1 H), 2.45 (ddd, $^{3}J = 10.9$, $^{3}J = 8.8$, $^{3}J = 7.4$ Hz, 1 H), AB-signal ($\delta_A = 2.25$, $\delta_B = 2.01$, $J_{AB} = 12.8$ Hz, additionally split by $^{3}J_{(A)} = 7.4$, $^{4}J_{(A)} = 2.1$ Hz and $^{3}J_{(B)} = 10.9$ Hz, 2 H), 1.86 (dd, $^{2}J = 13.2$, $^{3}J \approx 7.6$ Hz, 1 H), 1.33−1.66 (m, 10 H), 1.24 (t, $^{3}J = 7.1$ Hz, 3 H), 1.22 (t, $^{3}J = 7.1$ Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): δ = 172.1, 171.4, 83.5, 71.3, 63.1, 61.5, 61.4, 50.9, 43.2, 40.4, 35.1, 35.1, 33.2, 26.0, 23.8, 23.2, 14.2 (2 C) ppm. IR (film): $\tilde{\nu}$ = 2935, 1730, 1445, 1365, 1250, 1180, 1070, 1030, 920, 860 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{18}H_{28}O_5^{+\cdot}$: 324.1937; found 324.1934 [M$^{+\cdot}$].

**Diethyl 2-(2-Cycloheptylideneethyl)-2-(oxiranyl)methylmalonate (18):** Table 3, Entry 3: According to GP 1: NaH [293 mg (95%), 11.6 mmol, 1.39 equiv.], diethyl 2-(oxiranyl)methylmalonate (1.95 g, 9.03 mmol, 1.08 equiv.) and 2-(bromoethylidene)cycloheptane[68] (1.70 g, 8.37 mmol) were allowed to react in dry THF (50 mL) for 4 h at 0 °C. After silica gel chromatography (CyH/EtOAc, 92:8) combined with bulb-to-bulb distillation (236 °C, 1.1 mbar) **18** (986 mg, 35%) was isolated as a colorless liquid. $R_f$ (CyH/EtOAc, 89:11) = 0.31. $^{1}$H NMR (400 MHz, CDCl$_3$): δ = 4.97 (t, pseudo-quint, $^{3}J = 7.2$, $^{4}J = 1.4$ Hz, 1 H), AB-signal ($\delta_{A1} = 4.20$, $\delta_{B1} = 4.16$, $J_{AB} = 10.8$ Hz, additionally split by $^{3}J = 7.1$ Hz, 2 H), 4.19 (q, $^{3}J = 7.1$ Hz, 2 H), 2.96 (dddd, $^{3}J = 6.5$, $^{3}J = 5.3$, $^{3}J = 3.9$, $^{3}J = 2.7$ Hz, 1 H), AB-signal ($\delta_{A2} = 2.73$, $\delta_{B2} = 2.68$, $J_{AB} = 15.2$ Hz, additionally split by $^{3}J = 7.2$ Hz, 2 H), 2.71 (dd, $^{2}J = 5.2$, $^{3}J = 3.9$ Hz, 1 H), 2.41 (dd, $^{2}J = 5.2$, $^{3}J = 2.7$ Hz, 1 H), 2.22−2.26 (m, 2 H), 2.16−2.18 (m, 2 H), AB-signal ($\delta_{A3} = 2.11$, $\delta_{B3} = 2.04$, $J_{AB} = 14.5$ Hz, additionally split by $^{3}J_{(A3)} = 5.3$ Hz and $^{3}J_{(B3)} = 6.5$ Hz, 2 H), 1.45−1.59 (m, 8 H), 1.25 (t, $^{3}J = 7.1$ Hz, 3 H), 1.24 (t, $^{3}J = 7.1$ Hz, 3 H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 171.3, 145.6, 117.8, 61.5, 61.4, 56.5, 48.8, 47.0, 38.1, 36.2, 31.7, 30.3, 29.9, 29.4, 29.3, 27.0, 14.1 ppm. IR (film): $\tilde{\nu}$ = 2980, 2925, 2850, 1730, 1445, 1365, 1285, 1210, 1095, 1035, 860 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{19}H_{30}O_5^{+\cdot}$: 338.2093; found 338.2091 [M$^{+\cdot}$].

**Diethyl Spiro[cycloheptane-1,2′-(3′-oxabicyclo[3.3.0]octane)]-7′,7′-dicarboxylate (19):** Table 3, Entry 3: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [Cp$_2$TiCl$_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **18** (338 mg, 1.00 mmol) in dry ethyl acetate (50 mL) were allowed to react for 16 h at room temperature. After silica gel chromatography (CyH/EtOAc, 95:5) **19** (210 mg, 62%) was obtained as a colorless liquid which contained trace amounts of polymeric impurities (< 3%). $R_f$ (CyH/EtOAc, 89:11) = 0.25. $^{1}$H NMR (400 MHz, CDCl$_3$): δ = AB-signal ($\delta_{A1} = 4.19$, $\delta_{B1} = 4.16$, $J_{AB} = 10.6$ Hz, additionally split by $^{3}J = 7.1$ Hz, 2 H), 4.14 (q, $^{3}J = 7.1$ Hz, 2 H), 3.82 (dd, $^{2}J = 9.2$, $^{3}J = 7.9$ Hz, 1 H), 3.51 (dd, $^{2}J = 9.2$, $^{3}J = 3.6$ Hz, 1 H), 2.83 (ddddd, $^{3}J \approx 8.9$, $^{3}J = 8.7$, $^{3}J = 7.9$, $^{3}J \approx 7.4$, $^{3}J = 3.6$ Hz, 1 H), 2.62 (ddd, $^{2}J = 13.3$, $^{3}J = 8.7$, $^{4}J = 2.1$ Hz, 1 H), 2.45 (ddd, $^{3}J = 11.2$, $^{3}J \approx 8.9$, $^{3}J = 7.2$ Hz, 1 H), AB-signal ($\delta_{A2} = 2.23$, $\delta_{B2} = 1.99$, $J_{AB} = 12.8$ Hz, additionally split by $^{3}J_{(A2)} = 7.2$, $^{3}J_{(A2)} = 2.1$ Hz, and $^{3}J_{(B2)} = 11.2$ Hz, 2 H), 1.85 (dd, $^{2}J = 13.3$, $^{3}J \approx 7.4$ Hz, 1 H), 1.27−1.87 (m, 12 H), 1.24 (t, $^{3}J = 7.1$ Hz, 3 H), 1.22 (t, $^{3}J = 7.1$ Hz, 3 H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 172.0, 171.4, 87.1, 71.9, 63.0, 61.5, 61.4, 53.1, 43.1, 40.4, 37.7, 36.5, 35.6, 29.7, 29.3, 23.4, 22.3, 14.2 ppm. IR (film): $\tilde{\nu}$ = 2925, 2860, 1730, 1460, 1365, 1255, 1175, 1105, 1070, 860 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{19}H_{30}O_5^{+\cdot}$: 338.2093; found 338.2093 [M$^{+\cdot}$]. $C_{19}H_{30}O_5$ (338.4): calcd. C 67.43, H 8.93; found C 67.28, H 8.62.

**Diethyl 2-(3-Ethylpent-2-enyl)-2-(oxiranyl)methylmalonate (20):** Table 3, Entry 4: According to GP 1: NaH [220 mg (95%), 8.71 mmol, 1.45 equiv.], diethyl 2-(oxiranyl)methylmalonate (1.56 g, 7.22 mmol, 1.20 equiv.) and 1-bromo-3-ethylpent-2-ene[68] (1.06 g, 6.00 mmol) were allowed to react at 0 °C in dry THF (50 mL). While warming to room temperature, the reaction mixture was stirred for 16 h. After silica gel chromatography (CyH/EtOAc, 92:8) **20** (1.33 g, 71%) was isolated as a colorless liquid.

$R_f$ (CyH/EtOAc, 89:11) = 0.24. $^{1}$H NMR (400 MHz, CDCl$_3$): δ = 4.91 (tm, $^{3}J = 7.3$ Hz, 1 H), 4.12−4.23 (m, 2 H), 4.19 (q, $^{3}J = 7.1$ Hz, 2 H), 2.96 (dddd, $^{3}J \approx 6.7$, $^{3}J = 5.2$, $^{3}J = 4.0$, $^{3}J = 2.7$ Hz, 1 H), 2.67−2.78 (m, 3 H), 2.41 (dd, $^{2}J = 5.2$, $^{3}J = 2.7$ Hz, 1 H), AB-signal ($\delta_A = 2.09$, $\delta_B = 2.03$, $J_{AB} = 14.6$ Hz, additionally split by $^{3}J_{(A)} = 5.2$ Hz and $^{3}J_{(B)} \approx 6.7$ Hz, 2 H), 1.96−2.05 (m, 4 H), 1.24 (tm, $^{3}J = 7.1$ Hz, 6 H), 0.94 (tm, $^{3}J = 7.5$ Hz, 3 H), 0.94 (tm, $^{3}J = 7.6$ Hz, 3 H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 171.2, 147.2, 115.6, 61.5, 61.4, 56.6, 48.7, 47.0, 36.2, 31.6, 29.4, 23.3, 14.1, 13.1, 13.0 ppm. IR (film): $\tilde{\nu}$ = 2965, 2935, 1730, 1465, 1365, 1285, 1215, 1095, 1030, 930, 860 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{17}H_{28}O_5^{+\cdot}$: 312.1937; found 312.1916 [M$^{+\cdot}$]. $C_{17}H_{28}O_5$ (312.4): calcd. C 65.36, H 9.03; found C 65.22, H 9.08.

**Diethyl 2,2-Diethyl-3-oxabicyclo[3.3.0]octane-7,7-dicarboxylate (21):** Table 3, Entry 4: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [Cp$_2$TiCl$_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Mn (110 mg, 2.00 mmol, 2.00 equiv.) and **20** (312 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react for 16 h at room temperature. After silica gel chromatography (CyH/EtOAc, 90:10) **21** (202 mg, 64%) was obtained as a colorless liquid.

$R_f$ (CyH/EtOAc, 89:11) = 0.31. $^{1}$H NMR (400 MHz, CDCl$_3$): δ = 4.18 (q, $^{3}J = 7.2$ Hz, 2 H), 4.15 (q, $^{3}J = 7.1$ Hz, 2 H), 4.15 (q, $^{3}J = 7.2$ Hz, 1 H), 3.82 (dd, $^{2}J = 9.2$, $^{3}J \approx 7.8$ Hz, 1 H), 3.50 (dd, $^{2}J = 9.2$, $^{3}J = 3.8$ Hz, 1 H), 2.86 (ddddd, $^{3}J \approx 8.5$, $^{3}J \approx 8.4$, $^{3}J \approx 7.8$, $^{3}J \approx 7.5$, $^{3}J = 3.8$ Hz, 1 H), 2.60 (ddd, $^{2}J = 13.4$, $^{3}J \approx 8.4$, $^{4}J = 1.8$ Hz, 1 H), 2.39 (ddd, $^{3}J \approx 10.9$, $^{3}J \approx 8.5$ Hz, $^{3}J \approx 7.9$ Hz, 1 H), AB-signal ($\delta_A = 2.27$, $\delta_B = 2.03$, $J_{AB} = 12.7$ Hz, additionally split by $^{3}J_{(A)} \approx 7.9$, $^{4}J_{(A)} = 1.8$ Hz and $^{3}J_{(B)} \approx 10.9$ Hz, 2 H), 1.85 (dd, $^{2}J = 13.4$, $^{3}J \approx 7.5$ Hz, 1 H), 1.69 (dq, $^{2}J = 14.5$, $^{3}J \approx 7.5$ Hz, 1 H), 1.41−1.52 (m, 2 H), 1.35 (dq, $^{2}J = 14.5$, $^{3}J \approx 7.5$ Hz, 1 H), 1.24 (t, $^{3}J = 7.2$ Hz, 3 H), 1.22 (t, $^{3}J = 7.1$ Hz, 3 H), 0.84 (t, $^{3}J = 7.6$ Hz, 3 H), 0.79 (t, $^{3}J \approx 7.5$ Hz, 3 H ) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 172.0, 171.4, 87.1, 71.8, 63.1, 61.5, 51.2, 43.5, 40.2, 35.2, 26.5, 24.8, 14.2, 9.2, 7.7 ppm. IR (film): $\tilde{\nu}$ = 2970, 1730, 1460, 1365, 1255, 1180, 1070, 1035, 915, 860 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{15}H_{23}O_5^{+}$: 283.1546; found 283.1537 [M − $C_2H_5^{+}$]. $C_{17}H_{28}O_5$ (312.4): calcd. C 65.36, H 9.03; found C 65.30, H 8.95.

**Diethyl 2-(4-Methylpent-3-enyl)-2-(oxiranyl)methylmalonate (22):** Table 3, Entry 5: A suspension of NaH [300 mg (95%), 11.9 mmol, 1.29 equiv.] in dry DMF (40 mL) was cooled to 0 °C and diethyl 2-(oxiranyl)methylmalonate (2.00 g, 9.26 mmol) was slowly added. When deprotonation was complete 5-iodo-2-methylpent-2-ene[69] (3.00 g, 14.3 mmol, 1.54 equiv.) dissolved in dry DMF (10 mL) was added and the reaction mixture was stirred for 60 h while warming to room temperature. The reaction was quenched by the addition of MTBE (100 mL) and water (30 mL). The organic layer was separated and washed with water (5  30 mL) and satd. aq. NaCl (30 mL). After drying ($MgSO_4$), the solvent was evaporated under vacuum. Silica gel chromatography (CyH/EtOAc, 92:8) of the residue combined with bulb-to-bulb distillation (210 °C, 1.4 mbar) delivered **22** (2.25 g, 81%) as a colorless liquid which contained trace amounts (< 5%) of an unknown impurity. $R_f$ (CyH/EtOAc, 89:11) = 0.29. $^{1}H$ NMR (400 MHz, $CDCl_3$, contains 2% cyclohexane): $\delta = 5.07$ (tm, $^{3}J = 7.0$ Hz, 1 H), AB-signal ($\delta_{A1} = 4.21$, $\delta_{B1} = 4.17$, $J_{AB} = 10.7$ Hz, additionally split by $^{3}J = 7.1$ Hz, 2 H), 4.18 (q, $^{3}J = 7.1$ Hz, 2 H), 2.94 (dddd, $^{3}J = 6.6$, $^{3}J \approx 4.7$, $^{3}J \approx 4.1$, $^{3}J \approx 2.5$ Hz, 1 H), 2.72 (dd, $^{2}J = 5.0$, $^{3}J \approx 4.1$ Hz, 1 H), 2.42 (dd, $^{2}J = 5.0$, $^{3}J \approx 2.5$ Hz, 1 H), AB-signal ($\delta_{A2} = 2.17$, $\delta_{B2} = 2.02$, $J_{AB} = 14.4$ Hz, additionally split by $^{3}J_{(A2)} \approx 4.7$ Hz and $^{3}J_{(B2)} = 6.6$ Hz, 2 H), 1.80–2.02 (m, 4 H), 1.65 (s, 3 H), 1.56 (s, 3 H), 1.24 (t, $^{3}J = 7.1$ Hz, 6 H ) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$, contains 2% cyclohexane): $\delta = 171.3$, 132.7, 123.1, 61.5, 61.4, 56.4, 48.7, 46.8, 36.1, 33.4, 25.7, 23.0, 17.7, 14.1 ppm. IR (film): $\tilde{\nu} = 2980$, 1730, 1445, 1365, 1220, 1095, 1095, 1025, 925, 860 $cm^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{16}H_{26}O_5^{+\cdot}$: 298.1780; found 298.1775 [$M^{+\cdot}$]. $C_{16}H_{26}O_5$ (298.4): calcd. C 64.41, H 8.78; found C 64.57, H 8.65.

**Diethyl 7,7-Dimethyl-8-oxabicyclo[4.3.0]nonane-3,3-dicarboxylate (23):** Table 3, Entry 5: According to GP 2: Collidine hydrochloride (79.0 mg, 0.50 mmol, 0.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Mn (11.0 mg, 0.20 mmol, 0.20 equiv.) and **22** (298 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react for 24 h at room temperature. After silica gel chromatography (CyH/EtOAc, 92:8) **23** (187 mg, 62%) was obtained as a mixture of diastereoisomers (87:13). $R_f$ (CyH/EtOAc, 89:11) = 0.21. $^{1}H$ NMR (400 MHz, $CDCl_3$): $\delta = 4.11$–4.26 (m, 2 H)$^{B}$, AB-signal ($\delta_{A1} = 4.22$, $\delta_{B1} = 4.18$, $J_{AB} = 10.8$ Hz, additionally split by $^{3}J \approx 7.2$ Hz, 2 H)$^{A}$, 4.14 (q, $^{3}J \approx 7.2$ Hz, 2 H)$^{B}$, 4.13 (q, $^{3}J \approx 7.2$ Hz, 2 H)$^{A}$, 3.89 (pseudo-t, $^{2}J \approx {}^{3}J \approx 7.5$ Hz, 1 H)$^{A}$, 3.84 (dd, $^{2}J \approx 8.8$, $^{3}J = 7.5$ Hz, 1 H)$^{B}$, 3.48 (dd, $^{2}J \approx 8.8$, $^{3}J = 6.6$ Hz, 1 H)$^{B}$, 3.30 (dd, $^{3}J = 10.6$, $^{2}J \approx 7.5$ Hz, 1 H)$^{A}$, 2.51–2.53, 2.48–2.49 (m, 4 H)$^{A,B}$, AB-signal ($\delta_{A1} = 2.18$, $\delta_{B1} = 1.97$, $J_{AB} = 14.2$ Hz, additionally split by $^{3}J_{(A1)} = 5.9$ Hz and $^{3}J_{(B1)} = 8.7$ Hz, 2 H)$^{B}$, 2.12–2.21 (m, 1 H)$^{B}$, 1.94–1.99 (m, 1 H)$^{B}$, 1.79–1.91 (m, 2 H)$^{A,B}$, 1.63–1.69 (m, 2 H)$^{A}$, 1.52 (pseudo-t, $^{2}J = {}^{3}J = 12.7$ Hz, 1 H)$^{A}$, 1.16–1.36 (m, 3 H)$^{A,B}$, 1.24 (t, $^{3}J \approx 7.2$ Hz, 6 H)$^{A,B}$, 1.22 (s, 3 H)$^{A}$, 1.20 (t, $^{3}J \approx 7.2$ Hz, 6 H)$^{A,B}$, 1.16 (s, 3 H)$^{B}$, 1.15 (s, 3 H)$^{B}$, 0.95 (s, 3 H)$^{A}$ ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$) **(major isomer)**: $\delta = 172.2$, 171.0, 81.3, 70.7, 61.6, 61.4, 55.1, 54.0, 40.1, 33.4, 31.7, 28.2, 23.9, 23.0, 14.2, 14.1; **(minor isomer)**: $\delta = 172.3$, 172.1, 82.6, 70.0, 61.4, 52.9, 45.1, 36.2, 30.2, 29.2, 28.6, 24.5, 20.2, 14.1 ppm. IR (film): $\tilde{\nu} = 2970$, 1730, 1450, 1365, 1235, 1180, 1095, 1015, 840, 640 $cm^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{16}H_{26}O_5^{+\cdot}$: 298.1780; found 298.1791 [$M^{+\cdot}$]. $C_{16}H_{26}O_5$ (298.4): calcd. C 64.41, H 8.78; found C 64.28, H 8.75.

**Diethyl 2-(3-Methylpent-2-enyl)-2-(oxiranyl)methylmalonate (24):** Table 3, Entry 6: According to GP 1: NaH [353 mg (95%), 14.0 mmol, 1.43 equiv.], diethyl 2-(oxiranyl)methyl malonate (2.16 g, 10.0 mmol, 1.02 equiv.) and 1-bromo-3-methylpent-2-ene[70] (1.60 g, 9.82 mmol) were allowed to react at 0 °C in dry THF (50 mL). While warming to room temperature, the reaction mixture was stirred for 16 h. After silica gel chromatography (CyH/EtOAc, 94:6) combined with bulb-to-bulb distillation (210 °C, 1.4 mbar) a colorless liquid was isolated containing **24** (1.99 g, 68%) as mixture of diastereoisomers [(*E*)/(*Z*), 74:26]. $R_f$ (CyH/EtOAc, 89:11) = 0.33. $^{1}H$ NMR (400 MHz, [$D_6$]benzene): $\delta = 5.23$ (t, pseudo-sext, $^{3}J = 7.4$, $^{4}J \approx 1.1$ Hz, 1 H)$^{A}$, 5.16–5.20 (tm, $^{3}J = 7.3$ Hz, 1 H)$^{B}$, 3.95–4.10 (m, 4 H)$^{B}$, AB-signal ($\delta_{A1} = 4.05$, $\delta_{B1} = 3.99$, $J_{AB} = 10.7$ Hz, additionally split by $^{3}J = 7.1$ Hz, 2 H)$^{A}$, 4.02 (q, $^{3}J = 7.1$ Hz, 2 H)$^{A}$, 2.97–3.03 (m, 6 H)$^{A,B}$, AB-signal ($\delta_{A} = 2.37$, $\delta_{B} = 2.10$, $J_{AB} = 14.6$ Hz, additionally split by $^{3}J_{(A)} = 4.3$ Hz and $^{3}J_{(B)} = 7.5$ Hz, 2 H)$^{B}$, AB-signal ($\delta_{A2} = 2.36$, $\delta_{B2} = 2.11$, $J_{AB} = 14.5$ Hz, additionally split by $^{3}J_{(A2)} = 4.3$, $^{3}J_{(B2)} = 7.1$ Hz, 2 H)$^{A}$, 2.33 (dd, $^{2}J = 5.2$, $^{3}J = 3.8$ Hz, 1 H)$^{B}$, 2.33 (dd, $^{2}J = 5.3$, $^{3}J = 3.8$ Hz, 1 H)$^{A}$, 2.09 (dd, $^{2}J = 5.2$, $^{3}J = 2.8$ Hz, 1 H)$^{B}$, 2.09 (dd, $^{2}J = 5.3$, $^{3}J = 2.6$ Hz, 1 H)$^{A}$, 1.97 (qd, $^{3}J = 7.5$, $^{4}J = 2.2$ Hz, 2 H)$^{B}$, 1.89 (qm, $^{3}J = 7.5$ Hz, 2 H)$^{A}$, 1.59 (q, $^{4}J = 1.4$ Hz, 3 H)$^{B}$, 1.52 (d, $^{4}J \approx 1.1$ Hz, 3 H)$^{A}$, 0.96 (t, $^{3}J = 7.1$ Hz, 6 H)$^{A,B}$, 0.95 (t, $^{3}J = 7.1$ Hz, 6 H)$^{A,B}$, 0.90 (t, $^{3}J = 7.5$ Hz, 3 H)$^{A}$, 0.85 (t, $^{3}J = 7.5$ Hz; 3 H)$^{B}$. $^{13}C$ NMR (100 MHz, [$D_6$]benzene): $\delta = 171.1^{A,B}$, $171.0^{A,B}$, $141.2^{B}$, $141.1^{A}$, $118.1^{B}$, $117.2^{A}$, $61.3^{B}$, $61.2^{B}$, $61.3^{A}$, $61.2^{A}$, $57.1^{A}$, $56.9^{B}$, $48.5^{A}$, $48.5^{B}$, $46.3^{A}$, $46.2^{B}$, $36.9^{A,B}$, $33.0^{A}$, $32.6^{A}$, $32.3^{B}$, $25.2^{B}$, $23.2^{B}$, $16.2^{A}$, $14.1^{A,B}$, $13.0^{A}$, $12.7^{B}$ ppm. IR (film): $\tilde{\nu} = 2965$, 1730, 1445, 1365, 1285, 1220, 1095, 1030, 860 $cm^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{16}H_{26}O_5^{+\cdot}$: 298.1780; found 298.1777 [$M^{+\cdot}$]. $C_{16}H_{26}O_5$ (298.4): calcd. C 64.41, H 8.78; found C 64.42, H 8.72.

**Diethyl 2-Ethyl-2-methyl-3-oxabicyclo[3.3.0]octane-7,7-dicarboxylate (25):** Table 3, Entry 6: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Mn (110 mg, 2.00 mmol, 2.00 equiv.) and **24** (298 mg, 1.00 mmol) as a 74:26 mixture of isomers in dry THF (10 mL) were allowed to react for 16 h at room temperature. After silica gel chromatography (CyH/EtOAc, 93:7) **25** (191 mg, 63%) was obtained as a 64:36 mixture of diastereoisomers. At 0 °C (16 h) **25** (195 mg, 65%) was obtained. At −20 °C **25** (117 mg, 39%) was obtained after 72 h.

$R_f$ (CyH/EtOAc, 89:11) = 0.19. $^{1}H$ NMR (300 MHz, $CDCl_3$): $\delta = 4.17$ (q, $^{3}J \approx 7.1$ Hz, 2 H)$^{A,B}$, 4.15 (q, $^{3}J \approx 7.1$ Hz, 2 H)$^{A,B}$, 3.92 (dd, $^{2}J = 9.0$, $^{3}J = 8.0$ Hz, 1 H)$^{B}$, 3.80 (dd, $^{2}J = 9.1$, $^{3}J = 7.7$ Hz, 1 H)$^{A}$, 3.54 (dd, $^{2}J = 9.0$, $^{3}J = 3.6$ Hz, 1 H)$^{B}$, 3.51 (dd, $^{2}J = 9.1$, $^{3}J = 3.7$ Hz, 1 H)$^{A}$, 2.78–2.95 (m, 2 H)$^{A,B}$, 2.62 (ddd, $^{2}J = 13.3$, $^{3}J = 8.6$, $^{4}J = 2.0$ Hz, 1 H)$^{B}$, 2.60 (ddd, $^{2}J = 13.3$, $^{3}J = 8.6$, $^{4}J = 2.1$ Hz, 1 H)$^{A}$, 2.42 (ddd, $^{3}J = 10.9$, $^{3}J = 9.2$, $^{3}J = 7.5$ Hz, 1 H)$^{A}$, 2.39 (ddd, $^{3}J = 11.0$, $^{3}J = 9.0$, $^{3}J \approx 7.9$ Hz, 1 H)$^{B}$, AB-signal ($\delta_{A} = 2.27$, $\delta_{B} = 2.00$, $J_{AB} = 12.8$ Hz, additionally split by $^{3}J_{(A)} \approx 7.9$, $^{4}J_{(A)} = 2.0$ Hz and $^{3}J_{(B)} = 11.0$ Hz, 2 H)$^{B}$, AB-signal ($\delta_{A} = 2.24$, $\delta_{B} = 2.02$, $J_{AB} = 12.9$ Hz, additionally split by $^{3}J_{(A)} = 7.5$, $^{4}J_{(A)} = 2.1$ Hz and $^{3}J_{(B)} = 10.9$ Hz, 2 H)$^{A}$, 1.86 (dd, $^{2}J = 13.3$, $^{3}J = 7.4$ Hz, 2 H)$^{A,B}$, 1.27–1.70 (m, 4 H)$^{A,B}$, 1.24 (t, $^{3}J = 7.2$ Hz, 3 H)$^{A}$, 1.24 (t, $^{3}J = 7.2$ Hz, 3 H)$^{B}$, 1.22 (t, $^{3}J \approx 7.1$ Hz, 3 H)$^{A}$, 1.22 (t, $^{3}J \approx 7.1$ Hz, 3 H)$^{B}$, 1.15 (s, 3 H)$^{A}$, 1.08 (s, 3 H)$^{B}$, 0.91 (t, $^{3}J = 7.5$ Hz, 3 H)$^{B}$, 0.83 (t, $^{3}J = 7.4$ Hz, 3 H)$^{A}$ ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 172.0^{B}$, $172.0^{A}$, $171.3\ ^{A,B}$, $84.7^{B}$, $84.1^{A}$, $72.1^{B}$, $71.7^{A}$, $63.2^{A}$, $63.0^{B}$, $61.5\ ^{A,B}$, $61.44\ ^{A,B}$, $52.2^{B}$, $51.8^{A}$, $43.7^{A}$, $43.2^{B}$, $40.4^{A}$, $40.3^{B}$, $36.0^{A}$, $35.4^{B}$, $31.6^{A}$, $29.8^{B}$, $22.8^{B}$, $20.1^{A}$, $14.2\ ^{A,B}$, $9.5^{B}$, $8.4^{A}$ ppm. IR (film): $\tilde{\nu} = 2975$, 2875, 1730, 1465, 1365, 1255, 1100, 1070, 1035, 875 $cm^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{16}H_{26}O_5^{+\cdot}$: 298.1780; found 298.1795 [$M^{+\cdot}$]. $C_{16}H_{26}O_5$ (298.4): calcd. C 64.41, H 8.78; found C 64.52, H 8.68.

**Diethyl 2-(3-Isopropyl-4-methylpent-2-enyl)-2-(oxiranyl)methylmalonate (26):** Table 3, Entry 7: According to GP 1: NaH [144 mg (95%), 5.70 mmol, 1.14 equiv.], diethyl 2-(oxiranyl)methylmalonate (1.08 g, 5.00 mmol) and 1-bromo-3-isopropyl-4-methylpent-2-

ene[70] (1.02 g, 5.00 mmol, 1.00 equiv.) were allowed to react at 0 °C in dry THF (20 mL). While warming to room temperature, the reaction mixture was stirred for 16 h. After silica gel chromatography (CyH/EtOAc, 94:6) **26** (1.36 g, 80%) was isolated as a colorless liquid.

$R_f$ (CyH/EtOAc, 89:11) = 0.36. $^{1}$H NMR (300 MHz, $CDCl_3$): δ = 4.94 (t, $^{3}J = 7.4$ Hz, 1 H), 4.10−4.25 (m, 2 H), 4.19 (q, $^{3}J = 7.1$ Hz, 2 H), 2.97 (dddd, $^{3}J = 6.5$, $^{3}J = 5.3$, $^{3}J = 4.0$, $^{3}J = 2.6$ Hz, 1 H), 2.82 (sept, $^{3}J \approx 6.9$ Hz, 1 H), 2.76 (dd, $^{3}J = 7.4$, $^{5}J = 1.7$ Hz, 2 H), 2.70 (dd, $^{2}J = 5.1$, $^{3}J = 4.0$ Hz, 1 H), 2.40 (dd, $^{2}J = 5.1$, $^{3}J = 2.6$ Hz, 1 H), 2.28 (sept, $^{3}J \approx 6.9$ Hz, 1 H), AB-signal ($\delta_A = 2.08$, $\delta_B = 2.01$, $J_{AB} = 14.5$ Hz, additionally split by $^{3}J_{(A)} = 5.3$ Hz and $^{3}J_{(B)} = 6.5$ Hz, 2 H), 1.24 (t, $^{3}J = 7.1$ Hz, 6 H), 0.96 (d, $^{3}J \approx 6.9$ Hz; 12 H ) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 171.2, 155.8, 114.0, 61.5, 61.4, 56.6, 48.7, 47.0, 36.2, 31.2, 29.5, 28.3, 24.8, 24.8, 21.1, 21.0, 14.1 ppm. IR (film): ṽ = 2960, 2870, 1730, 1465, 1365, 1285, 1190, 1095, 1030, 855 cm$^{-1}$. HRMS (70 eV, EI): *m/z*: calcd. for $C_{19}H_{32}O_5^{+\cdot}$: 340.2250; found 340.2254 [$M^{+\cdot}$]. $C_{19}H_{32}O_5$ (340.5): calcd. C 67.03, H 9.47; found C 66.82, H 9.42.

**2-(3-Methylbut-2-enyl)-2-(oxiranyl)methyl-1,3-dithiane (28):** Table 3, Entry 8: To a mixture of 2-(3-methylbut-2-enyl)-1,3-dithiane, 2-(2-methylbut-3-en-2-yl)-1,3-dithiane and 1,3-dithiane (1.39 g, 7.80 mmol) in dry THF (40 mL) at −20 °C, *n*BuLi [9.00 mL (1.50 M in tetrahydrofuran), 6.00 mmol, 0.77 equiv.] was added dropwise and the reaction was stirred for 90 min at the same temperature. After cooling to −78 °C epibromohydrin (1.10 g, 8.00 mmol, 1.03 equiv.) was added and stirring was continued for 2 h at −20 °C. The reaction was quenched by pouring the mixture into water (100 mL), the organic layer was separated and the aqueous phase was extracted with PE (3 30 mL). The combined organic layers were washed with water (2 30 mL) and satd. aq. NaCl (20 mL) and dried ($MgSO_4$). After silica gel chromatography (CyH/EtOAc, 90:10) **28** (314 mg, 16%) was obtained as a colorless oil. $R_f$ (CyH/EtOAc, 89:11) = 0.35. $^{1}$H NMR (400 MHz, $CDCl_3$): δ = 5.29 (t, pseudo-sept, $^{3}J \approx 7.1$, $^{4}J = 1.5$ Hz, 1 H), 3.18 (tdd, $^{3}J \approx 5.5$, $^{3}J = 4.0$, $^{3}J = 2.7$ Hz, 1 H), 2.82−2.91 (m, 4 H), 2.78 (dd, $^{2}J = 5.1$, $^{3}J = 4.0$ Hz, 1 H), AB-signal ($\delta_{A1} = 2.71$, $\delta_{B1} = 2.67$, $J_{AB} = 15.3$ Hz, additionally split by $^{3}J_{(A1)} = 7.2$, $^{5}J_{(A1)} = 0.9$, $^{3}J_{(B1)} = 7.0$ Hz and $^{5}J_{(B1)} = 1.1$ Hz, 2 H), 2.52 (dd, $^{2}J = 5.1$, $^{3}J = 2.7$ Hz, 1 H), AB-signal ($\delta_{A2} = 2.17$, $\delta_{B2} = 2.08$, $J_{AB} = 14.9$ Hz, additionally split by $^{3}J_{(A2)} = 5.7$, $^{3}J_{(B2)} = 5.4$ Hz, 2 H), 1.90−2.04 (m, 2 H), 1.74 (pseudo-q, $^{4}J \approx {}^{5}J \approx 1.3$ Hz, 3 H), 1.66 (d, $^{4}J = 1.0$ Hz, 3 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 135.4, 118.4, 52.5, 49.3, 47.2, 41.5, 38.4, 26.4, 25.2, 26.1, 18.5 ppm. IR (film): ṽ = 2910, 1670, 1440, 1375, 1275, 1125, 985, 910, 830, 675 cm$^{-1}$. HRMS (70 eV, EI): *m/z*: calcd. for $C_{12}H_{20}OS_2^{+\cdot}$: 244.0956; found 244.0962 [$M^{+\cdot}$].

**2′,2′-Dimethylspiro[1,3-dithiane-2,7′-(3′-oxabicyclo[3.3.0]octane)] (29):** Table 3, Entry 8: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (49.8 mg, 0.20 mmol, 0.20 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **28** (244 mg, 1.00 mmol) in dry ethyl acetate (50 mL) were allowed to react for 60 h at room temperature. After silica gel chromatography (CyH/EtOAc, 90:10) **29** (161 mg, 65%) was obtained as a slightly yellow liquid.

$R_f$ (CyH/EtOAc, 89:11) = 0.25. $^{1}$H NMR (400 MHz, $CDCl_3$): δ = 3.93 (dd, $^{2}J = 9.1$, $^{3}J \approx 7.9$ Hz, 1 H), 3.56 (dd, $^{2}J = 9.1$, $^{3}J \approx 3.3$ Hz, 1 H), 3.00 (dd*pseudo*-td, $^{3}J \approx 8.8$, $^{3}J = 8.5$, $^{3}J \approx 7.9$, $^{3}J \approx 3.3$ Hz, 1 H), 2.77−2.94 (m, 4 H), 2.67 (ddd, $^{3}J = 10.9$, $^{3}J \approx 8.8$, $^{3}J \approx 7.3$ Hz, 1 H), 2.64 (ddd, $^{2}J = 13.5$, $^{3}J = 8.5$, $^{4}J = 2.4$ Hz, 1 H), 2.33 (ddd, $^{2}J = 13.0$, $^{3}J \approx 7.3$, $^{4}J = 2.4$ Hz, 1 H), 1.96−2.03 (m, 2 H), 1.83 (dd, $^{2}J = 13.0$, $^{3}J = 10.9$ Hz, 1 H), 1.75 (dd, $^{2}J = 13.5$, $^{3}J \approx 7.9$ Hz, 1 H), 1.24 (s, 3 H), 1.16 (s, 3 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 81.4, 71.9, 57.3, 53.0, 48.3, 43.6, 42.8, 29.0, 27.8, 26.8, 25.9, 24.0 ppm. IR (film): ṽ = 2965, 1435, 1365, 1280, 1240, 1135, 1055, 1015, 990, 910, 815 cm$^{-1}$. HRMS (70 eV, EI): *m/z*: calcd. for $C_{12}H_{20}OS_2^{+\cdot}$: 244.0956; found 244.0951 [$M^{+\cdot}$]. $C_{12}H_{20}OS_2$ (244.4): calcd. C 58.97, H 8.25, S 26.23; found C 59.11, H 8.25, S 26.14.

**Diethyl 3-Oxabicyclo[3.3.0]octane-7,7-dicarboxylate (31):**[24] Table 4, Entry 1: According to GP 2: Collidine hydrochloride (788 mg, 5.00 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (49.8 mg, 0.20 mol, 0.10 equiv.), Zn (260 mg, 4.00 mmol, 2.00 equiv.) and **30**[24] (512 mg, 2.00 mmol) in dry THF (20 mL) were allowed to react for 20 h at room temperature. After silica gel chromatography (CyH/EtOAc, 93:7) **31** (26.7 mg, 5%) was obtained as a colorless liquid.

**Diethyl 2-But-2-enyl-2-(oxiranyl)methylmalonate (32):** Table 4, Entry 2: According to GP 1: NaH [253 mg (95%), 10.0 mmol, 1.00 equiv.], diethyl 2-(oxiranyl)methylmalonate (2.16 g, 10.0 mmol) and (*E*)-but-2-enyl mesylate, obtained by the mesylation of 2-butenol (1.08 g, 15.0 mmol) with mesyl chloride[71] (1.72 g, 15.0 mmol, 1.00 equiv.), were allowed to react at 0 °C in dry THF (30 mL). While warming to room temperature, the reaction mixture was stirred for 15 h. After silica gel chromatography (CyH/EtOAc, 93:7) combined with bulb-to-bulb distillation (100 °C, 1.6 mbar) a colorless liquid was isolated containing **32** (0.87 g, 32%) as a mixture of diastereoisomers [(*E*):(*Z*) > 95:5]. $R_f$ (CyH/EtOAc, 89:11) = 0.19. $^{1}$H NMR (300 MHz, $CDCl_3$): δ = 5.53 (dqt, $^{3}J = 15.0$, $^{3}J = 6.4$, $^{4}J = 1.2$ Hz, 1 H), 5.25 (dtq, $^{3}J = 15.0$, $^{3}J = 7.5$, $^{4}J = 1.6$ Hz, 1 H), AB-signal ($\delta_{A1} = 4.21$, $\delta_{B1} = 4.16$, $J_{AB} = 10.7$ Hz, additionally split by $^{3}J = 7.2$ Hz, 2 H), 4.18 (q, $^{3}J = 7.2$ Hz, 2 H), 2.95 (dddd, $^{3}J = 6.7$, $^{3}J \approx 5.0$, $^{3}J \approx 4.1$, $^{3}J \approx 2.4$ Hz, 1 H), 2.71 (dd, $^{2}J = 5.1$, $^{3}J \approx 4.1$ Hz, 1 H), 2.67 (dd, $^{3}J = 7.5$, $^{4}J = 1.2$ Hz, 2 H), 2.42 (dd, $^{2}J = 5.1$, $^{3}J \approx 2.4$ Hz, 1 H), AB-signal ($\delta_{A2} = 2.10$, $\delta_{B2} = 1.98$, $J_{AB} = 14.6$ Hz, additionally split by $^{3}J_{(A2)} \approx 5.0$ Hz and $^{3}J_{(B2)} = 6.7$ Hz, 2 H), 1.62 (dm, $^{3}J = 6.4$ Hz, 3 H), 1.25 (t, $^{3}J = 7.2$ Hz, 3 H), 1.24 (t, $^{3}J = 7.2$ Hz, 3 H ) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 171.0, 130.3, 124.5, 61.5, 56.6, 48.6, 47.0, 36.8, 35.9, 18.1, 14.2 ppm. IR (film): ṽ = 2985, 1730, 1445, 1365, 1210, 1130, 1035, 970, 925, 860 cm$^{-1}$. HRMS (70 eV, EI): *m/z*: calcd. for $C_{14}H_{22}O_5^{+\cdot}$: 270.1467; found 270.1466 [$M^{+\cdot}$]. $C_{14}H_{22}O_5$ (270.3): calcd. C 62.20, H 8.20; found C 61.96, H 8.12.

**Diethyl 2-Methyl-3-oxabicyclo[3.3.0]octane-7,7-dicarboxylate (33):** Table 4, Entry 2: According to GP 2: Collidine hydrochloride (197 mg, 1.25 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (24.9 mg, 0.10 mmol, 0.20 equiv.), Zn (65.0 mg, 1.00 mmol, 2.00 equiv.) and **32** (135 mg, 0.50 mmol) in dry ethyl acetate (25 mL) were allowed to react for 72 h at room temperature. After silica gel chromatography (CyH/EtOAc, 88:12) **33** (85.0 mg, 62%) was isolated as an inseparable 80:20 mixture of diastereoisomers. $R_f$ (CyH/EtOAc, 89:11) = 0.17. **Major Isomer:** $^{1}$H NMR (400 MHz, $CDCl_3$): δ = 4.17 (q, $^{3}J = 7.1$ Hz, 2 H), 4.16 (q, $^{3}J = 7.1$ Hz, 2 H), 3.98 (dd, $^{2}J = 9.0$, $^{3}J \approx 7.5$ Hz, 1 H), 3.76 (qd, $^{3}J = 6.2$, $^{3}J = 5.2$ Hz, 1 H), 3.51 (dd, $^{2}J = 9.0$, $^{3}J \approx 4.8$ Hz, 1 H), 2.85 (ddddd, $^{3}J = 9.7$, $^{3}J \approx 8.1$, $^{3}J \approx 7.5$, $^{3}J \approx 7.3$, $^{3}J \approx 4.8$ Hz, 1 H), 2.49 (ddd, $^{2}J \approx 13.3$, $^{3}J \approx 8.1$, $^{4}J = 1.3$ Hz, 1 H), 2.46 (ddd, $^{2}J \approx 13.3$, $^{3}J = 8.3$, $^{4}J = 1.3$ Hz, 1 H), 2.37 (dddd, $^{3}J = 9.7$, $^{3}J = 8.3$, $^{3}J \approx 7.0$, $^{3}J = 5.2$ Hz, 1 H), 1.99 (ddd, $^{2}J \approx 13.3$, $^{3}J \approx 7.3$, $^{3}J \approx 7.0$ Hz, 2 H), 1.23 (t, $^{3}J = 7.1$ Hz, 3 H), 1.23 (t, $^{3}J = 7.1$ Hz, 3 H), 1.16 (d, $^{3}J = 6.2$ Hz, 3 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 172.0, 171.4, 81.5, 72.8, 63.9, 61.6, 61.5, 51.5, 44.7, 39.2, 38.1, 19.8, 14.2. **Minor Isomer:** $^{1}$H NMR (400 MHz, $CDCl_3$): δ = 4.13−4.20 (m, 4 H), 3.70 (qd, $^{3}J = 6.2$, $^{3}J \approx 5.8$ Hz, 1 H), AB-signal ($\delta_{A1} = 3.64$, $\delta_{B1} = 3.58$, $J_{AB} =$

9.2 Hz, additionally split by $^3J_{(A1)} \approx 2.0$ Hz and $^3J_{(B1)} = 6.8$ Hz, 2 H), 2.77 (ddddd, $^3J = 9.6$, $^3J = 8.5$, $^3J \approx 8.3$, $^3J = 6.8$, $^3J \approx 2.0$ Hz, 1 H), 2.61 (dddd, $^3J \approx 10.4$, $^3J = 9.6$, $^3J = 7.8$, $^3J \approx 5.8$ Hz, 1 H), 2.60 (ddd, $^2J = 13.0$, $^3J = 8.5$, $^4J = 2.2$ Hz, 1 H), AB-signal ($\delta_{A2} = 2.20$, $\delta_{B2} = 1.97$, $J_{AB} = 12.9$ Hz, additionally split by $^3J_{(A2)} = 7.8$, $^4J_{(A2)} = 2.2$ Hz and $^3J_{(B2)} \approx 10.4$ Hz, 2 H), 1.81 (dd, $^2J = 13.0$, $^3J \approx 8.3$ Hz, 1 H), 1.24 (t, $^3J = 7.0$ Hz, 3 H), 1.22 (t, $^3J = 7.1$ Hz, 3 H), 1.16 (d, $^3J = 6.2$ Hz, 3 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 171.9, 171.2, 77.1, 73.7, 62.8, 61.4, 47.3, 43.9, 41.0, 34.3, 15.4, 14.1. **Mixture of Isomers:** IR (film): ṽ = 2975, 1730, 1445, 1365, 1255, 1180, 1070, 1030, 860 cm$^{-1}$. HRMS (70 eV, EI): *m/z*: calcd. for $C_{14}H_{22}O_5^{+\cdot}$: 270.1467; found 270.1468 [$M^{+\cdot}$]. $C_{14}H_{22}O_5$ (270.3): calcd. C 62.20, H 8.20; found C 61.91, H 8.17.

**Diethyl 2-Cyclopent-2-enyl-2-(oxiranyl)methylmalonate (34):** Table 4, Entry 3: According to GP 1: NaH (106 mg, 4.42 mmol, 2.00 equiv.), diethyl 2-(oxiranyl)methylmalonate (475 mg, 2.20 mmol, 1.00 equiv.), and 3-bromocyclopentene (904 mg, 6.15 mmol, 2.80 equiv.) were allowed to react in dry DMF (10 mL) at 0 °C. While warming to room temperature, the mixture was stirred for 3 h. After Silica gel chromatography (CyH/EtOAc, 94:6) 2-cyclopent-2-enyl-2-(oxiranyl)methylmalonic acid diethyl ester (372 mg, 60%) was isolated as a colorless liquid. $R_f$ (CyH/EtOAc, 94:6) = 0.3. $^1$H NMR (400 MHz, $CDCl_3$): δ = 5.78−5.70 (m, 2 H), 4.23−4.10 (m, 4 H), 3.51−3.42 (m, 1 H), 3.08−2.99 (m, 1 H), 2.72−2.65 (m, 1 H), 2.45−2.33 (m, 1 H), 2.30−2.19 (m, 2 H), 2.12−1.91 (m, 3 H), 1.74−1.60 (m, 1 H), 1.26−1.19 (m, 6 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): 170.9, 170.8, 170.7, 132.7, 132.4, 131.2, 131.0, 61.3, 61.1, 59.6, 50.2, 49.0, 47.3, 47.2, 36.3, 36.2, 31.8, 25.4, 25.3, 14.1, 14.0 ppm. IR (film): ṽ = 3450, 3050, 2985, 1730, 1445, 1370, 1225, 1160, 1095, 1035, 920, 860, 725 cm$^{-1}$. HRMS: calcd: 282.1467; found 282.1474.

**Diethyl 3-Oxatricyclo[5.2.1.0$^{4,10}$]decane-8,8-dicarboxylate (35):** Table 4, Entry 3: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (50 mg, 0.20 mmol, 0.20 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **34** (282 mg, 1.00 mmol, 1.00 equiv.) in dry ethyl acetate (50 mL) were allowed to react overnight at room temperature. Silica gel chromatography yielded **35** (169 mg, 60%) as a colorless liquid.

$R_f$ (CyH/EtOAc, 94:6) = 0.3. $^1$H NMR (400 MHz, $CDCl_3$): δ = 4.14 (m, 5 H), 3.63 (dd, $^2J = 8.9$, $^3J = 0.6$ Hz, 1 H), 3.43 (dd, $^2J = 9.0$, $^3J = 4.8$ Hz, 1 H), 3.12 (ddd, $^3J = 9.1$, $^3J = 9.1$, $^3J = 6.2$ Hz, 1 H), 2.93 (dddd, $^3J = 10.1$, $^3J = 8.7$, $^3J = 7.4$, $^4J = 1.3$ Hz, 1 H), 2.54 (dddd, $^3J = 10.1$, $^3J = 9.7$, $^3J = 8.1$, $^3J = 4.8$ Hz, 1 H), 2.26 (ddd, $^2J = 13.6$, $^3J = 8.2$, $^4J = 1.4$ Hz, 1 H), 2.11 (dd, $^2J = 13.6$, $^3J = 10.6$ Hz, 1 H), 1.93 (dd, $^2J = 12.7$, $^3J = 5.4$ Hz, 1 H), 1.57 (dd, $^3J = 12.7$, $^3J = 5.4$ Hz, 1 H), 1.48−1.30 (m, 2 H), 1.17 (dt, $^3J = 7.1$, $^3J = 2.3$ Hz, 6 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): 172.1, 169.9, 85.3, 72.9, 65.7, 61.3, 61.1, 54.9, 49.4, 43.2, 37.5, 33.1, 26.7, 14.1, 14.0 ppm. IR (film): ṽ = 3460, 2970, 1730, 1465, 1370, 1265, 1180, 1115, 1065, 1040, 1000, 945, 895, 860, 800 cm$^{-1}$. HRMS: calcd: 282.1467; found 282.1464.

**Diethyl 2-(Cyclohex-2-enyl)-2-(oxiranyl)methylmalonate (36):** Table 4, Entry 4: According to GP 1: NaH [404 mg (95%), 16.0 mmol, 1.17 equiv.], 2-(oxiranyl)methylmalonic acid diethyl ester (2.96 g, 13.7 mmol) and 1-bromocyclohex-2-ene [2.86 g (90%), 16.0 mmol, 1.17 equiv.] were allowed to react at 0 °C in dry THF (50 mL). While warming to room temperature, the reaction mixture was stirred for 16 h. After silica gel chromatography (CyH/EtOAc, 89:11) **36** (2.20 g, 54%) was isolated as a mixture of diastereoisomers (*dr* = 50:50). $R_f$ (CyH/EtOAc, 89:11) = 0.14. $^1$H NMR (400 MHz, $CDCl_3$): δ = 5.64−5.76 (m, 4 H)$^{A,B}$, 4.11−4.27 (m, 8 H)$^{A,B}$, 3.11 (dddd, $^3J = 5.9$, $^3J = 5.5$, $^3J \approx 3.8$, $^3J = 2.7$ Hz, 1 H), 3.04 (tdd, $^3J \approx 5.7$, $^3J \approx 3.8$, $^3J = 2.7$ Hz, 1 H), 2.94−3.01 (m, 2 H)$^{A,B}$, 2.71 (dd, $^2J = 5.1$, $^3J \approx 3.8$ Hz, 1 H), 2.70 (dd, $^2J = 5.1$, $^3J \approx 3.8$ Hz, 1 H), 2.43 (dd, $^2J = 5.1$, $^3J = 2.7$ Hz, 1 H), 2.41 (dd, $^2J = 5.1$, $^3J = 2.7$ Hz, 1 H), AB-signal ($\delta_{A1} = 2.11$, $\delta_{B1} = 2.05$, $J_{AB} = 14.6$ Hz, additionally split by $^3J_{(A1)} = 5.9$ Hz and $^3J_{(B1)} = 5.5$ Hz, 2 H), AB-signal ($\delta_{(A1)} = 2.09$, $\delta_{(B1)} = 2.04$, $J_{AB} = 14.5$ Hz, additionally split by $^3J \approx 5.7$ Hz, 2 H), 1.86−1.99 (m, 4 H)$^{A,B}$, 1.71−1.82 (m, 4 H)$^{A,B}$, 1.47−1.60 (m, 2 H)$^{A,B}$, 1.40−1.42 (m, 2 H)$^{A,B}$, 1.26 (t, $^3J = 7.1$ Hz, 3 H), 1.25 (t, $^3J = 7.0$ Hz, 3 H), 1.24 (t, $^3J = 7.1$ Hz, 3 H), 1.23 (t, $^3J = 7.0$ Hz, 3 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 170.7, 170.6, 170.5, 129.1, 128.7, 128.1, 127.7, 61.4, 61.3, 61.2, 60.0, 59.7, 49.2, 47.7, 47.5, 40.48, 40.42, 35.9, 35.8, 25.0, 24.7, 24.6, 22.5, 14.2, 14.1 ppm. IR (film): ṽ = 2935, 1730, 1445, 1365, 1225, 1095, 1030, 925, 860, 725 cm$^{-1}$. HRMS (70 eV, EI): *m/z*: calcd. for $C_{16}H_{24}O_5^{+\cdot}$: 296.1621; found 296.1624 [$M^{+\cdot}$]. $C_{16}H_{24}O_5$ (296.4): calcd. C 64.72, H 8.32; found C 64.84, H 8.16.

**Diethyl 3-Oxatricyclo[6.2.1.0$^{4,11}$]undecane-9,9-dicarboxylate (37):** Table 4, Entry 4: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (49.8 mg, 0.20 mmol, 0.20 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **36** (296 mg, 1.00 mmol) in dry ethyl acetate (50 mL) were allowed to react for 16 h at room temperature. After silica gel chromatography (CyH/EtOAc, 91:9) **37** (188 mg, 63%) was obtained as a colorless liquid. $R_f$ (CyH/EtOAc, 1:1) = 0.84. $^1$H NMR (400 MHz, $CDCl_3$): δ = AB-signal ($\delta_{A1} = 4.20$, $\delta_{B1} = 4.14$, $J_{AB} = 10.7$ Hz, additionally split by $^3J = 7.1$ Hz, 2 H), AB-signal ($\delta_{A2} = 4.19$, $\delta_{B2} = 4.10$, $J_{AB} = 10.8$ Hz, additionally split by $^3J = 7.1$ Hz, 2 H), 3.74 (ddd, $^3J \approx 7.3$, $^3J = 4.6$, $^3J = 2.6$ Hz, 1 H), AB-signal ($\delta_{A3} = 3.67$, $\delta_{B3} = 3.50$, $J_{AB} = 9.0$ Hz, additionally split by $^3J_{(A3)} = 1.6$ Hz and $^3J_{(B3)} = 6.5$ Hz, 2 H), 2.84 (ddd, $^3J = 9.9$, $^3J = 7.6$, $^3J \approx 7.3$ Hz, 1 H), 2.60−2.69 (m, 1 H), 2.65 (ddddd, $^3J = 9.9$, $^3J = 9.9$, $^3J = 8.4$, $^3J = 6.5$, $^3J = 1.6$ Hz, 1 H), AB-signal ($\delta_{A4} = 2.36$, $\delta_{B4} = 2.16$, $J_{AB} = 13.6$ Hz, additionally split by $^3J_{(A4)} = 8.4$, $^4J_{(A4)} = 1.0$ Hz and $^3J_{(B4)} = 9.9$ Hz, 2 H), 1.82−1.91 (m, 1 H), 1.65−1.76 (m, 2 H), 1.29−1.41 (m, 2 H), 1.17−1.26 (m, 1 H), 1.23 (t, $^3J = 7.1$ Hz, 3 H), 1.22 (t, $^3J = 7.1$ Hz, 3 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 172.0, 169.8, 76.9, 72.5, 67.5, 61.4, 61.2, 45.7, 43.6, 42.6, 38.4, 22.8, 21.1, 17.8, 14.2 ppm. IR (film): ṽ = 2955, 2865, 1730, 1460, 1365, 1250, 1200, 1070, 1030, 925, 860 cm$^{-1}$. HRMS (70 eV, EI): *m/z*: calcd. for $C_{16}H_{24}O_5^{+\cdot}$: 296.1624; found 296.1624 [$M^{+\cdot}$]. $C_{16}H_{24}O_5$ (296.4): calcd. C 64.84, H 8.16; found C 64.63, H 8.06.

**Diethyl 2-Cyclooct-2-enyl-2-(oxiranyl)methylmalonate (38):** Table 4, Entry 5: According to GP 1: NaH (180 mg, 7.50 mmol, 1.50 equiv.), diethyl 2-(oxiranyl)methylmalonate (1.08 mg, 5.00 mmol, 1.00 equiv.), and 3-bromocyclooctene[72] (1.32 mg, 7.00 mmol, 1.4 equiv.) were allowed to react in dry DMF (10 mL) at 0 °C. While warming to room temperature, the mixture was stirred for 3 h. After silica gel chromatography (CyH/EtOAc, 95:5) **38** (972 mg, 60%) was isolated as a colorless liquid. $R_f$ (CyH/EtOAc, 95:5) = 0.4. $^1$H NMR (400 MHz, $CDCl_3$): δ = 5.66 (dt, $^3J = 9.3$, $^3J = 9.2$ Hz, 1 H), 5.45−5.28 (m, 1 H), 4.23−4.08 (m, 4 H), 3.28−3.12 (m, 1 H), 2.64 (t, $^3J = 4.36$ Hz, 1 H), 2.37 (dd, $^3J = 4.8$ Hz, 1 H), 2.25−2.13 (m, 1 H), 2.09−1.93 (m, 3 H), 1.83−1.32 (m, 6 H), 1.28−1.05 (m, 9 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): 170.9, 170.6, 170.5, 131.2, 131.0, 129.1, 128.8, 61.3, 61.2, 61.1, 49.0, 48.8, 47.3, 47.2, 41.2, 40.3, 38.0, 37.5, 31.5, 31.4, 29.5, 26.5, 26.2, 25.9, 14.1, 14.0 ppm. IR (film): ṽ = 2930, 2855, 2360, 1730, 1445, 1370, 1200, 1115, 1025, 925, 860, 755, 715. HRMS: calcd: 324.1937; found 324.1930.

**Diethyl 3-Oxatricyclo[8.2.1.0$^{4,13}$]tridecane-11,11-dicarboxylate (39):** Table 4, Entry 5: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [Cp$_2$TiCl$_2$] (50 mg, 0.20 mmol, 0.20 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **38** (324 mg, 1.00 mmol, 1.00 equiv.) in dry ethyl acetate (50 mL) were allowed to react overnight at room temperature. Silica gel chromatography yielded **39** (236 mg, 73%) as a colorless liquid. $R_f$ (CyH/EtOAc, 95:5) = 0.3. $^1$H NMR (400 MHz, CDCl$_3$): δ = 4.13 (dq, $^3J$ = 10.8, $^3J$ = 7.2 Hz, 2 H), 4.07 (dq, $^3J$ = 10.8, $^3J$ = 7.1 Hz, 2 H), 3.51 (dd, $^2J$ = 9.0, $^3J$ = 1.13 Hz, 1 H), 3.45 (ddd, $^3J$ = 10.4, $^3J$ = 6.3, $^3J$ = 4.1 Hz, 1 H), 3.41 (dd, $^2J$ = 9.1, $^3J$ = 6.2 Hz, 1 H), 3.11 (tddd, $^3J$ = 9.8, $^3J$ = 8.6, $^3J$ = 6.2, $^3J$ = 1.2 Hz, 1 H), 2.51−2.31 (m, 3 H), 2.13−2.03 (m, 1 H), 1.89−1.63 (m, 4 H), 1.56−1.38 (m, 4 H), 1.18 (dt, $^3J$ = 7.2, $^3J$ = 3.8 Hz, 6 H), 1.15−0.75 (m, 2 H ) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): 171.6, 171.3, 82.3, 71.7, 66.4, 60.9, 60.5, 52.3, 46.4, 45.7, 50.0, 32.5, 25.8, 25.3, 24.9, 24.8, 14.1, 14.0 ppm. IR (film): ṽ = 3465, 2975, 1730, 1465, 1370, 1265, 1180, 1110, 1065, 1040, 1000, 945, 895, 860 cm$^{-1}$. HRMS: calcd: 324.1937; found 324.1939.

**2-(Cyclohex-2-enyl)-2-(oxiranyl)methyl-1,3-dithiane (40):** Table 4, Entry 6: To a solution of 2-cyclohex-2-enyl-1,3-dithiane (4.00 g, 20.00 mmol, 1.00 equiv.) in dry THF (100 mL) under argon at −20 °C, *n*BuLi (10.6 mL, 26 mmol, 1.30 equiv.) was added dropwise. Stirring was continued for 2 h and the anion cooled to −78 °C and quenched with epibromohydrin (3.98 g, 28.00 mmol, 1.40 equiv.). The reaction mixture was stirred at −20 °C for 3 h and then poured into water (200 mL) and the resulting mixture extracted with CH$_2$Cl$_2$ (300 mL). The organic layer was washed with water (2 × 50 mL) and brine (50 mL), dried with MgSO$_4$ and concentrated. Silica gel chromatography (5% Et$_2$O, 95% PE) yielded **40** (3.07 g, 60%) as a colorless liquid. $R_f$ (EtrO/PE, 5:95) = 0.29. $^1$H NMR (400 MHz, CDCl$_3$): δ = 5.95 (m, $^3J$ = 10.2 Hz, 1 H), 5.82 (m, $^3J$ = 10.2 Hz, 1 H), 3.27−3.20 (m, 1 H), 2.91−2.73 (m, 6 H), 2.53−2.48 (m, 1 H), 2.19−1.78 (m, 8 H), 1.60−1.41 (m, 2 H ) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): 130.0, 129.9, 127.2, 127.0, 56.4, 49.4, 49.3, 47.5, 42.1, 41.8, 38.9, 38.7, 26.0, 25.9, 25.8, 25.1, 25.0, 24.9, 24.8, 24.4, 22.7 ppm. IR (film): ṽ = 3485, 3025, 2925, 1645, 1420, 1345, 1270, 1140, 980, 910, 855, 830, 720, 685, 615. HRMS: calcd: 256.0956; found 256.0957.

**Spiro[1,3-dithiane-2,9′-(3′-oxatricyclo[6.2.1.0$^{4′,11′}$]undecane)] (41):** Table 4, Entry 6: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [Cp$_2$TiCl$_2$] (50 mg, 0.20 mmol, 0.20 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **40** (256 mg, 1.00 mmol, 1.00 equiv.) in dry ethyl acetate (50 mL) were allowed to react overnight at room temperature. Silica gel chromatography (6% Et$_2$O, 94% PE) yielded **41** (131 mg, 51%) as a colorless solid. M.p. 62 °C. $R_f$ (EtrO/PE, 6:94) = 0.4. $^1$H NMR (400 MHz, CDCl$_3$): δ = 3.77 (ddd, $^3J$ = 6.6, $^3J$ = 4.5, $^3J$ = 2.5 Hz, 1 H), 3.59 (dd, $^2J$ = 8.9, $^3J$ = 1.8 Hz, 1 H), 3.52 (dd, $^2J$ = 8.9, $^3J$ = 6.4 Hz, 1 H), 2.95 (dddd, $^3J$ = 9.9, $^3J$ = 8.3, $^3J$ = 6.4, $^3J$ = 1.8 Hz, 1 H), 2.88 (ddd, $^3J$ = 9.6, $^3J$ = 8.5, $^3J$ = 7.0 Hz, 1 H), 2.79 (dd, $^3J$ = 6.7, $^3J$ = 5.2 Hz, 2 H), 2.71 (dd, $^3J$ = 6.0, $^3J$ = 5.3 Hz, 2 H), 2.43 (ddd, $^2J$ = 13.3, $^3J$ = 8.3, $^4J$ = 1.3 Hz, 1 H), 2.25 (dddd, $^2J$ = 12.5, $^3J$ = 7.7, $^3J$ = 4.8, $^4J$ = 1.3 Hz, 1 H), 1.76 (dd, $^3J$ = 7.9, $^3J$ = 3.2 Hz, 1 H), 1.73 (dd, $^2J$ = 13.4, $^3J$ = 8.5 Hz, 1 H), 1.72 (dd, $^3J$ = 9.2, $^3J$ = 3.2 Hz, 1 H), 1.68−1.57 (m, 4 H), 1.40−1.25 (m, 2 H ) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): 76.7, 72.6, 61.9, 46.7, 45.8, 44.9, 44.3, 27.9, 27.7, 25.7, 22.5, 21.7, 18.1 ppm. IR (film): ṽ = 3450, 2940, 2865, 1425, 1360, 1305, 1250, 1225, 1185, 1100, 1075, 1050, 1000, 950, 905, 800, 675 cm$^{-1}$. HRMS: calcd: 256.0956; found 256.0954.

***trans*-4-Propyl-*cis*-3,7-dioxatricyclo[6.4.0.0$^{1,5}$]dodecane (43)**[34]: Table 4, Entry 7: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol), **42**[34] (210 mg, 1.00 mmol), Zn (135 mg, 2.00 mmol), [Cp$_2$TiCl$_2$] (24.9 mg, 100 µmol) in THF (10 mL) were allowed to react for 42 h. Purification by SiO$_2$ flash chromatography (5% EtOAc, 95% CyH to 12% EtOAc, 88% CyH) afforded the separation of **43** (105 mg, 50%) from a mixture of **44** and **45** (73.0 mg, 35%). The latter mixture was hydrogenated over Pd (10% on charcoal) and quantitatively transformed into **44**[34] (*dr* = 71:29).

**Diethyl 2-Phenyl-3-oxabicyclo[3.3.0]octane-7,7-dicarboxylate (47):** Table 5, Entry 1: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [Cp$_2$TiCl$_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Mn (110 mg, 2.00 mmol, 2.00 equiv.) and (*E*)-**46**[31] (332 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react for 16 h at room temperature. After silica gel chromatography (CyH/EtOAc, 95:5) **47** (33.1 mg, 10%) was obtained as a colorless liquid. Alternatively, collidine hydrochloride (79.0 mg, 0.50 mmol, 0.50 equiv.), [Cp$_2$TiCl$_2$] (24.9 mg, 0.10 mmol, 0.10 equiv.), Mn (11.0 mg, 0.20 mmol, 0.20 equiv.) and (*E*)-**46**[31] (332 mg, 1.00 mmol) in dry THF (10 mL) were allowed to react for 4 h at 70 °C. After silica gel chromatography **47** (57.7 mg, 17%) was isolated as a colorless liquid. $R_f$ (CyH/EtOAc, 1:1) = 0.71. $^1$H NMR (400 MHz, [D$_6$]benzene): δ = 7.32 (dm, $^3J$ ≈ 7.3 Hz, 2 H), 7.16 (pseudo-tm, $^3J$ ≈ 7.3 Hz, 2 H), 7.08 (tm, $^3J$ ≈ 7.3 Hz, 1 H), 4.68 (d, $^3J$ = 5.2 Hz, 1 H), 3.98 (q, $^3J$ ≈ 7.1 Hz, 2 H), 3.95 (q, $^3J$ ≈ 7.1 Hz, 1 H), 3.95 (q, $^3J$ ≈ 7.1 Hz, 1 H), 3.93 (dd, $^2J$ = 9.0, $^3J$ = 7.1 Hz, 1 H), 3.52 (dd, $^2J$ = 9.0, $^3J$ = 4.7 Hz, 1 H), 2.64−2.81 (m, 2 H), AB-signal ($\delta_A$ = 2.66, $\delta_B$ = 2.39, $J_{AB}$ = 13.2 Hz, additionally split by $^3J_{(A)}$ = 8.2, $^4J_{(A)}$ = 1.3 Hz and $^3J_{(B)}$ = 6.0 Hz, 2 H), 2.54 (ddd, $^2J$ = 13.2, $^3J$ = 8.1, $^4J$ = 1.3 Hz, 1 H), 2.16 (dd, $^2J$ = 13.2, $^3J$ = 7.2 Hz, 1 H), 0.94 (t, $^3J$ ≈ 7.1 Hz, 3 H), 0.91 (t, $^3J$ ≈ 7.1 Hz, 3 H ) ppm. $^{13}$C NMR (100 MHz, [D$_6$]benzene): δ = 171.7, 171.3, 142.8, 128.6, 127.4, 126.1, 86.8, 73.6, 64.0, 61.4, 53.1, 45.3, 39.4, 38.8, 14.1, 14.0 ppm. IR (film): ṽ = 2980, 1730, 1450, 1365, 1255, 1195, 1070, 1030, 755, 700 cm$^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{19}H_{24}O_5^{+\cdot}$: 332.1624; found 332.1633 [M$^{+\cdot}$].

**Diethyl (*E*)-2-[3-(4-Methoxyphenyl)prop-2-enyl]-2-(oxiranyl)methylmalonate (48):** Table 5, Entry 2: According to GP 1: NaH [353 mg (95%), 14.0 mmol, 1.17 equiv.], diethyl 2-(oxiranyl)methylmalonate (2.59 g, 12.0 mmol) and 1-(2-bromopropenyl)-4-methoxybenzene,[73] obtained by the bromination of (*E*)-3-(4-methoxyphenyl)prop-2-en-1-ol (2.00 g, 12.2 mmol), dissolved in dry THF (10 mL) were allowed to react at 0 °C in dry THF (30 mL). While warming to room temperature, the reaction mixture was stirred for 16 h. After silica gel chromatography (CyH/EtOAc, 92:8) (*E*)-**48** (2.08 g, 47%) was obtained as a slightly yellow oil which contained trace amounts (< 5%) of rearranged epoxide. $R_f$ (CyH/EtOAc, 89:11) = 0.18. $^1$H NMR (300 MHz, [D$_6$]benzene): δ = 7.19 (dm, $^3J$ = 8.7 Hz, 2 H), 6.72 (dm, $^3J$ = 8.7 Hz, 2 H), 6.43 (dm, $^3J$ = 15.6 Hz, 1 H), 6.14 (dt, $^3J$ = 15.6, $^3J$ ≈ 7.6 Hz, 1 H), 4.03 (q, $^3J$ = 7.1 Hz, 2 H), 4.02 (q, $^3J$ = 7.1 Hz, 2 H), 3.30 (s, 3 H), AB-signal ($\delta_A$ = 3.15, $\delta_B$ = 3.11, $J_{AB}$ = 14.2 Hz, additionally split by $^3J_{(A)}$ ≈ 7.5, $^4J_{(A)}$ ≈ 1.3, $^3J_{(B)}$ = 7.5, $^4J_{(B)}$ ≈ 1.2 Hz, 2 H), 2.99 (d, pseudo-td, $^3J$ = 7.6, $^3J$ ≈ 4.0, $^3J$ = 2.5 Hz, 1 H), AB-signal ($\delta_A$ = 2.41, $\delta_B$ = 2.10, $J_{AB}$ = 14.6 Hz, additionally split by $^3J_{(A)}$ ≈ 4.0, $^3J_{(B)}$ = 7.6 Hz, 2 H), 2.33 (dd, $^2J$ = 5.3, $^3J$ ≈ 4.0 Hz, 1 H), 2.08 (dd, $^2J$ = 5.3, $^3J$ = 2.5 Hz, 1 H), 0.96 (t, $^3J$ = 7.1 Hz, 3 H), 0.95 (t, $^3J$ = 7.1 Hz, 3 H ) ppm. $^{13}$C NMR (75 MHz, [D$_6$]benzene): δ = 170.9, 170.8, 159.8, 134.3, 130.4, 127.8, 122.0, 114.4, 61.4, 61.3, 57.4, 54.8, 48.5, 46.2, 37.9, 37.2, 14.1 ppm. IR (film): ṽ = 2980, 1730, 1605, 1510, 1465, 1250, 1210, 1035, 970, 840 cm$^{-1}$. HRMS (70 eV, EI):

*m*/*z*: calcd. for $C_{20}H_{26}O_6^{+\cdot}$: 362.1729; found 362.1733 [$M^{+\cdot}$]. $C_{20}H_{26}O_6$ (362.4): calcd. C 66.28, H 7.23; found C 66.18, H 7.40.

**Diethyl 2-(4-Methoxyphenyl)-3-oxabicyclo[3.3.0]octane-7,7-dicarboxylate (49):** Table 5, Entry 2: According to GP 2: Collidine hydrochloride (394 mg, 2.50 mmol, 2.50 equiv.), [$Cp_2TiCl_2$] (49.8 mg, 0.20 mmol, 0.20 equiv.), Zn (131 mg, 2.00 mmol, 2.00 equiv.) and **48** (362 mg, 1.00 mmol) in dry ethyl acetate (10 mL) were allowed to react for 16 h at room temperature. After silica gel chromatography (CyH/EtOAc, 75:25) **49** (189 mg, 52%) was obtained as a colorless yellow liquid containing trace amounts of an unknown impurity (< 5%). $R_f$ (CyH/EtOAc, 1:1) = 0.70. $^1$H NMR (400 MHz, $CDCl_3$): δ = AA′BB′-signal with centers at 6.86 and 7.24 (4 H), 4.61 (d, $^3J$ = 5.7 Hz, 1 H), 4.21 (q, $^3J$ = 7.1 Hz, 2 H), 4.19 (q, $^3J$ = 7.1 Hz, 1 H), 4.18 (q, $^3J$ = 7.1 Hz, 1 H), 4.13 (dd, $^2J$ = 9.0, $^3J \approx$ 7.6 Hz, 1 H), 3.79 (s, 3 H), 3.65 (dd, $^2J$ = 9.0, $^3J$ = 5.1 Hz, 1 H), 2.96 (ddddd, $^3J$ = 9.8, $^3J \approx$ 7.6, $^3J \approx$ 7.4, $^3J \approx$ 7.0, $^3J$ = 5.1 Hz, 1 H), 2.80 (dddd, $^3J$ = 9.8, $^3J \approx$ 8.0, $^3J$ = 7.0, $^3J$ = 5.7 Hz, 1 H), 2.57 (ddd, $^2J$ = 13.5, $^3J \approx$ 7.4, $^4J$ = 1.5 Hz, 1 H), 2.55 (ddd, $^2J$ = 13.5, $^3J$ = 7.0, $^4J$ = 1.5 Hz, 1 H), 2.29 (dd, $^2J$ = 13.5, $^3J \approx$ 7.0 Hz, 1 H), 2.11 (dd, $^2J$ = 13.5, $^3J \approx$ 8.0 Hz, 1 H), 1.27 (t, $^3J$ = 7.1 Hz, 3 H), 1.24 (t, $^3J$ = 7.1 Hz, 3 H ) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 171.9, 171.5, 159.2, 133.8, 127.3, 113.9, 86.5, 73.5, 63.8, 61.6, 55.4, 52.3, 45.1, 39.2, 38.2, 14.2, 14.1 ppm. IR (film): ṽ = 2980, 1730, 1610, 1515, 1365, 1250, 1175, 1035, 860, 825 $cm^{-1}$. HRMS (70 eV, EI): *m*/*z*: calcd. for $C_{20}H_{26}O_6^{+\cdot}$: 362.1729; found 362.1727 [$M^{+\cdot}$]. $C_{20}H_{26}O_6$ (362.4): calcd. C 66.28, H 7.23; found C 66.24, H 7.37.

## Acknowledgments

We are indebted to the Deutsche Forschungsgemeinschaft (Gerhard Hess-Programm), the Fonds der Chemischen Industrie (Dozentenstipendium to A. G.) for generous financial support. We also thank Mr. Hambloch, Institut für Organische Chemie, Universität Göttingen, Mrs. Bähr, Institut für Organische Chemie und Biochemie, Universität Freiburg, and Mrs. Martens, Kekulé-Institut für Organische Chemie und Biochemie, Universität Bonn for performing combustion analyses.

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Received January 2, 2004