DOI: 10.1002/ejoc.200500487

Cerium-Catalyzed, Aerobic Oxidative Synthesis of 1,2-Dioxane Derivatives from Styrene and Their Fragmentation into 1,4-Dicarbonyl Compounds

Michael Rössle,[a] Thomas Werner,[a] Wolfgang Frey,[a] and Jens Christoffers*[a]

Keywords: Catalysis / Cerium / Oxidation / 1,4-diketones / C–C bond formation / Peroxides

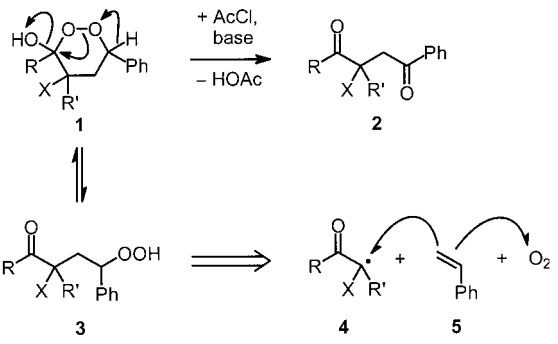
1,4-Diketones were prepared by cerium-catalyzed oxidative coupling of styrene with molecular oxygen and 1,3-dicarbonyl compounds. This two-step sequence was performed as a one-pot procedure without isolation of the intermediate products. The first step is a metal-catalyzed radical reaction yielding 3-hydroxy-1,2-dioxane derivatives being the cyclotautomers of initially formed 4-hydroperoxy ketones. In the second step of this sequence, these endoperoxides are converted with AcCl–pyridine by Kornblum–DeLaMare fragmentation into the 1,4-dicarbonyl motif. Several intermediate 1,2-dioxane derivatives could be isolated and structurally characterized by X-ray crystallography.

Introduction

In 1951 Kornblum and DeLaMare reported on base-induced fragmentations of dialkyl peroxides into ketones and alcohols.[1] Since then, this process has received much attention from synthetic organic chemists. Of particular interest is the selective conversion of endoperoxides to hydroxy ketones.[2] According to this fragmentation, 1,4-dicarbonyl compounds **2** are obtained after activation of the OH group by acetylation[3] from 3-hydroxy-1,2-dioxane derivatives **1**. The latter can be regarded as the cyclotautomers of γ-hydroperoxy ketones **3**. Therefore, a simple access of these peroxides could be the basis for a valuable synthetic route to 1,4-diketones,[4] an important structural motif for the preparation of heterocyclic compounds.[5]

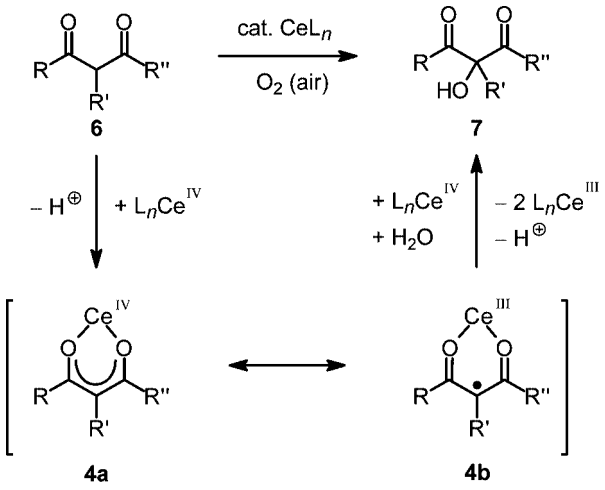
In contrast to 1,3- and 1,5-dicarbonyl compounds being accessible by Claisen or Michael reactions,[6] the synthesis of 1,4-dicarbonyl functionalized carbon skeletons requires an Umpolung strategy, carried out by either the classic utilization of α-halo ketones[7] or more modern strategies involving 1,3-dithian derivatives.[8] Both methodologies are multistep sequences and require stoichiometric amounts of reagents, such as halogen sources or bases. They are therefore with regard to economical and ecological considerations not very attractive. An atom-economic Umpolung strategy, however, is the use of the Stetter reagent or other organocatalytic systems.[9]

In order to contribute to the field of 1,4-dicarbonyl compounds **2**, we have developed a process leading to γ-hydroperoxy ketones **3** by attack of an α-radical **4** to styrene **5** (Scheme 1) and trapping of the intermediate radical by molecular oxygen.[10] This development is clearly a result of our earlier observation, that β-dicarbonyl compounds **6** are cleanly α-hydroxylated in the presence of molecular oxygen and catalytic amounts of cerium salts (Scheme 2).[11] Our mechanistic proposal for this α-hydroxylation process involves the formation of a radical species **4b** (X = ester or ketone) by ligand-to-metal charge-transfer of β-diketonato cerium(IV) complexes **4a** as shown in Scheme 2. While the overall mechanistic view of these processes is still not completely clear and presently under investigation in our laboratories, we aimed to utilize the radical species **4** for the C–C coupling reaction with styrene (**5**) (Scheme 1). A subsequent Kornblum–DeLaMare fragmentation leads to 1,4-dicarbonyl compounds **2**.[12] Oxidative coupling of styrene (**5**) might herein be regarded as an alternative to the application of phenacylhalides.[13]



Scheme 1. Transformation of 3-hydroxy-1,2-dioxane derivatives into 1,4-dicarbonyl compounds by Kornblum–DeLaMare fragmentation; R, R′ = alkyl, cycloalkyl; X = ester, ketone.

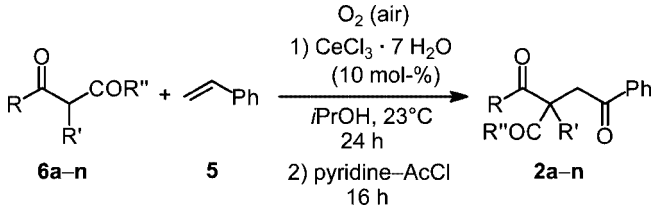
[a] Institut für Organische Chemie der Universität Stuttgart, Pfaffenwaldring 55, 70569 Stuttgart, Germany
Fax: +49-711-685-4269
E-mail: jchr@oc.uni-stuttgart.de



Scheme 2. Proposed mechanism for the cerium-catalyzed α-hydroxylation of β-dicarbonyl compounds **6**.

Results and Discussion

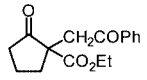
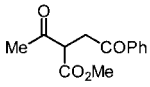
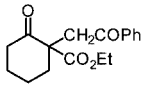
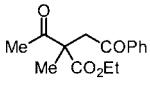
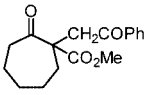
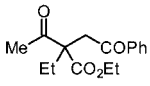
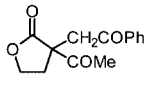
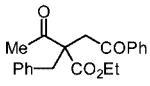
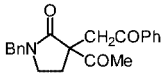
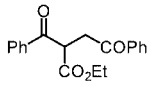
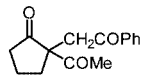
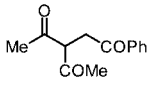
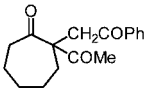
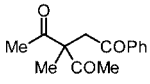
We have already reported on the reaction of β-dicarbonyl compounds **6** with styrene (**5**) in the presence of catalytic amounts of $CeCl_3 \cdot 7H_2O$ under an atmosphere of air, which gives γ-hydroperoxy ketones **3**.[10b] These ketones, however, were isolated as their cyclotautomeric 3-hydroxy-1,2-dioxane derivatives **1** with three stereogenic centers. Therefore, these materials were obtained as hardly separable mixtures of diastereoisomers, which is not acceptable from a preparative point of view. In order to transform these 1,2-dioxanes **1** to stereochemically unique materials we aimed to either oxidize or reduce the endoperoxidic moiety. After considerable experimental affords with several catalytically active transition metal compounds,[14] we finally focused on the Kornblum–DeLaMare fragmentation, which is in our hands best achieved with stoichiometric amounts of AcCl and pyridine. In order to circumvent the rather tedious isolation and purification procedure of the peroxides, we have developed a two-step one-flask procedure, which is summarized in Scheme 3. Use of atmospheric O_2 turned out to be optimal. If the partial pressure of oxygen is too high, the α-hydroxylation process becomes a significant side reaction and the respective alcohols **7** (Scheme 2) are obtained as byproducts.



Scheme 3. Formation of 1,4-dicarbonyl compounds **2** by a two-step one-pot reaction consisting of cerium-catalyzed C–C coupling with styrene (**5**) and subsequent Kornblum–DeLaMare fragmentation.

In Table 1 products **2** are listed together with their yields over two steps in the one-flask procedure. Acyclic (right column) and cyclic starting materials (left) have been investigated; yields for the latter are generally higher than for the acyclic compounds. For cyclic β-keto esters **6a**–**6c** as well as the α-acetylbutyrolactone (**6d**), -lactam (**6e**), and -cyclopentanone (**6f**) the yield of the diketone **2** was generally good and independent of the ring size. Yields of 61–87% over two steps implicate a range of 78–93% for each step. For the seven-membered ring diketone **2g** the yield significantly breaks down to 14%. From this product single crystals were grown, which were suitable for X-ray crystallographic analysis. An ORTEP representation of its molecular structure is given in Figure 1.[15] The large strain around the quaternary carbon atom is evidenced by the bending of the C1–O1 away from the acetyl group.

Table 1. List of products **2** and yields.

	Product	Yield[a]		Product	Yield[a]
2a		69%	**2h**		72%
2b		61%	**2i**		68%
2c		71%	**2j**		42%
2d		87%	**2k**		53%
2e		72%	**2l**		56%
2f		61%	**2m**		28%
2g		14%	**2n**		10%

[a] Total yield over two steps.

The best yield achieved for an acyclic product was 72% for β-keto ester **2h**. Yields for this class of substrates seem to be dependent on the steric demand of the α-alkyl substituent. This is illustrated by the decrease in the order H (**2h**), Me (**2i**),[16] Bn (**2k**),[17] Et (**2j**) from 72% to 42% yield. Replacement of the acetyl group in **2h** by a benzoyl residue in **2l**[18] lowered the yield from 72% to 56%. The α-isopropyl derivative did not give any product under these reaction conditions. The effect was even more drastic for the acetylacetone derivatives **2m**[19] and **2n**.[19] Introduction of the Me group resulted in a decrease from 28% to 10%. For the α-benzyl-substituted β-diketone no conversion was observed. In these cases, however, the low yields might also be due to the instability of the products **6** under basic reaction conditions. It is well known, that aliphatic 1,3-diketones tend to decompose according to a retro-Claisen reaction.

While peroxide formation from cyclic β-keto esters **6a**–**6c** as well as from lactone **6d** and lactam **6e** was reported earlier,[10b] respective experimental and characterization

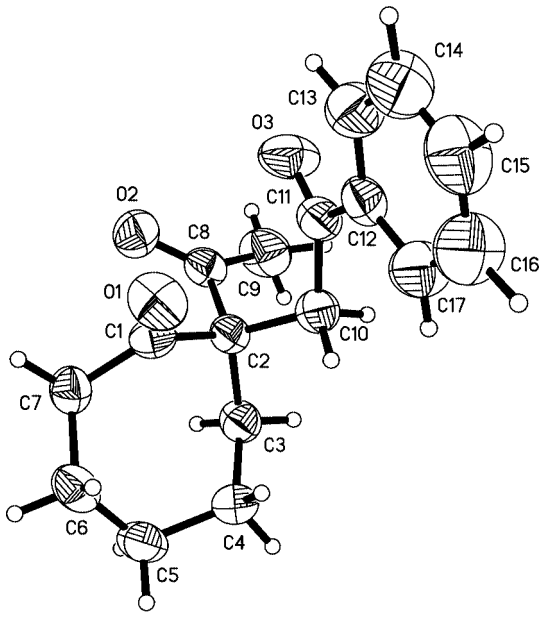
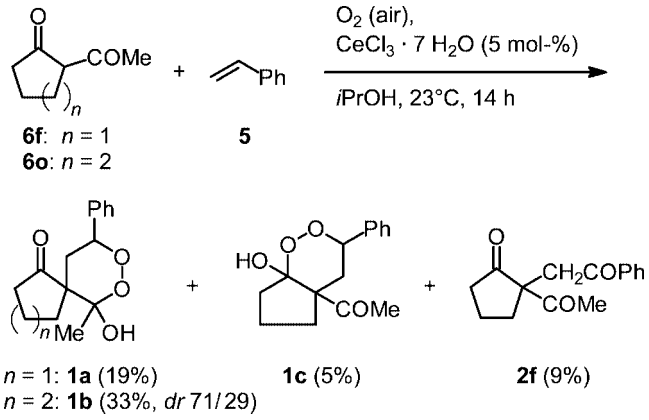


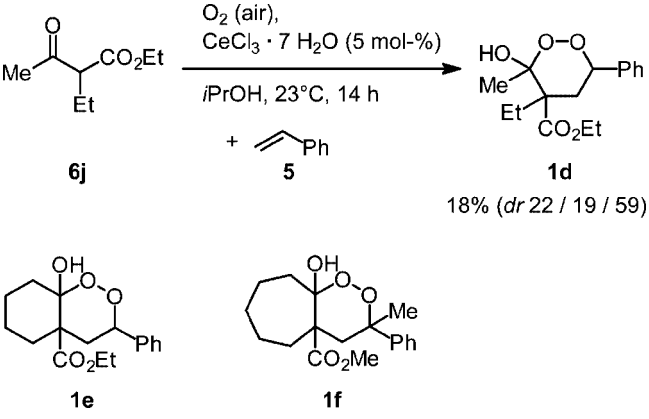
Figure 1. ORTEP view of the structure of triketone **2g** in the solid state.



Scheme 4. Conversion of α-acetylcycloalkanones to 1,2-dioxane derivatives **1**.

data for products of cyclic diketones as well as acyclic β-keto esters and β-diketones are included in this article. Conversion of α-acetylcyclopentanone (**6f**) and -cyclohexanone (**6o**) with 5 mol-% of cerium catalyst, an excess of styrene (**5**) and O_2 (air) gave spirocyclic 1,2-dioxane derivatives **1a** (19%) and **1b** (33%) as the major products (Scheme 4). In the case of the five-membered ring, an annulated cyclotautomer **1c** (5%) and the 1,4-diketone **2f** (9%) were isolated as byproducts. The constitution of the isomers **1a** and **1c** can be clearly assigned by the shifts in the ^1H NMR spectra. For the six-membered ring starting material **6o** no formation of a 1,4-diketone or an annulated 1,2-dioxane was observed, but **1b** was obtained as a mixture of two diastereoisomers (*dr* = 71:29). For all three 1,2-dioxanes **1a**, **1b**, and **1c** the relative configuration could not be assigned.

The only monocyclic 3-hydroxy-1,2-dioxane derivative we were able to characterize so far is compound **1d** (Scheme 5), which was prepared from β-keto ester **6j** by application of our standard protocol. Unfortunately, this material was obtained as a mixture of three diastereoisomers. Repeated chromatographic separations, however, lead to



Scheme 5. Synthesis of a monocyclic 1,2-dioxane **1d** and constitutions of annulated 1,2-dioxanes **1e** and **1f**.

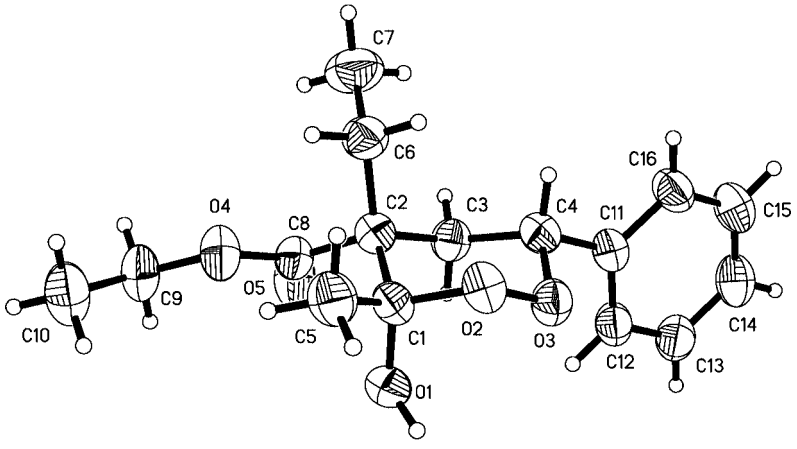


Figure 2. ORTEP view of the structure of monocyclic 1,2-dioxane **1d** in the solid state.

unique species, although this purification resulted in a very low overall yield (18%). We were able to grow single crystals that were suitable for X-ray structure analysis from one of these isomers. A representation of the molecular structure is given in Figure 2. The three larger substituents at each stereogenic center occupy equatorial positions (OH at C1, EtO_2C at C2, and Ph at C4, atom numbering according to Figure 2). The six membered ring is clearly in a chair conformation. Intermolecular H-bonding between the OH proton and the O3 oxygen atom of the peroxide unit is stabilizing the solid-state structure.

We thought that the conformation of the peroxo unit might be of interest. Fortunately, we were also able to grow single crystals of two other 1,2-dioxane derivatives **1e** and **1f**, which are annulated by a six- and seven-membered ring. The preparation of these compounds from β-keto esters **6b** respectively **6c** and styrene (**5**) and α-methylstyrene was reported earlier.[10b] Graphic representations of their solid-state structures are given in Figure 3 and Figure 4. Compound **1e** consists of two *cis*-annulated six-membered rings both in the chair conformation. The phenyl and the OH group are in equatorial conformation. In contrast to **1d** the intermolecular H-bond of compound **1f** is formed to the ester-carbonyl oxygen O5. In compound **1f** the six- and seven-membered rings are *trans*-annulated. In this case the H-bond is intermolecular. The 1,2-dioxane ring is in chair conformation, however, the phenyl group is in distorted axial position due to strain with the axial ester moiety and the axial lone pair at O3.

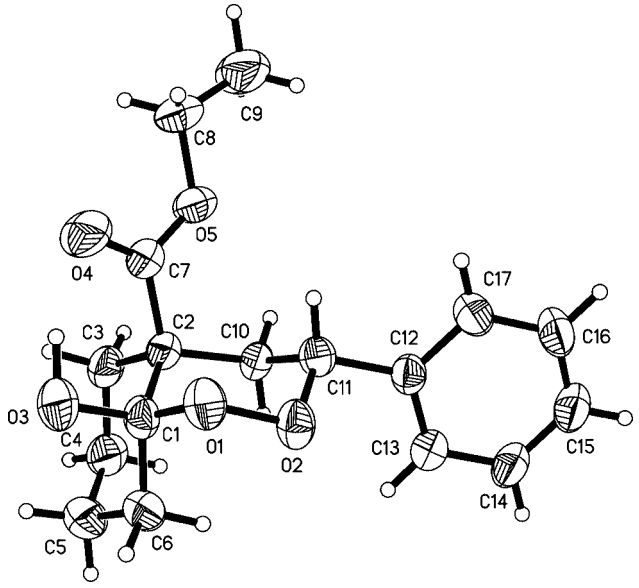


Figure 3. ORTEP view of the structure of *cis*-annulated 1,2-dioxane **1e** in the solid state.

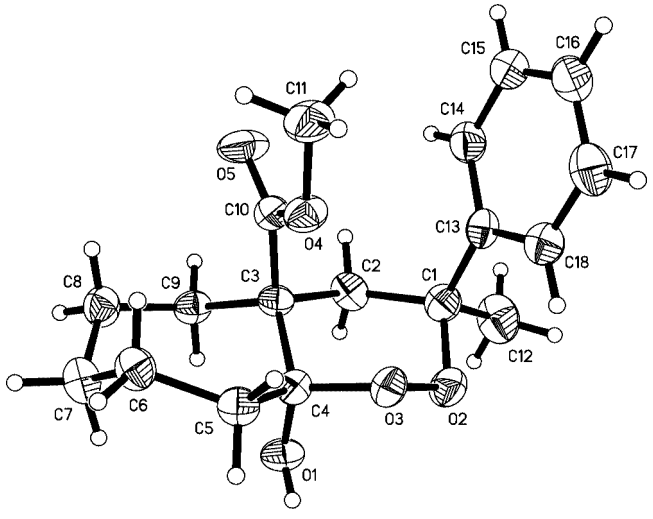


Figure 4. ORTEP view of the structure of *trans*-annulated 1,2-dioxane **1f** in the solid state.

Conclusions

In contrast to 1,3- and 1,5-dicarbonyl compounds, which are accessible by Claisen or Michael reaction, the direct synthesis of 1,4-dicarbonyl compounds is still a challenging task and commonly requires α-halogenation of ketones or other Umpolung strategies. With regard to atom economy, however, both methods are not optimal.

In the present publication we report on a cerium-catalyzed C–C coupling of 1,3-dicarbonyl compounds with styrene and oxygen yielding 4-hydroperoxy ketones, which exist as 3-hydroxy-1,2-dioxane derivatives. Base-induced Kornblum–DeLaMare fragmentation of these intermediate products afford compounds with a 1,4-dicarbonyl moiety. Since these endoperoxides are obtained as not easy to purify mixtures of diastereoisomers, this sequence is performed as a two-step one-pot procedure. Starting from simple starting materials and utilizing atmospheric oxygen as oxidant, these results can – in terms of economical and ecological considerations – be regarded as a starting point for further developments.

Experimental Section

General: Melting points were measured on a Büchi 510 and are uncorrected. Column chromatography was carried out using Merck SiO_2 60 with hexanes (PE, b.p. 40–60 °C) and ethyl acetate (EA) as eluents. ^1H NMR spectra were recorded on a Bruker ARX 500 (500 MHz) or a Bruker ARX 300 (300 MHz). ^{13}C NMR spectra were recorded on a Bruker ARX 500 (125 MHz), a Bruker ARX 300 (75 MHz) or a Bruker AC 250 (62 MHz). Multiplicities were determined with DEPT experiments. The β-dicarbonyl compounds **6a**, **6b**, **6c**, **6d**, **6f**, **6h**, **6l**, **6m**, **6n**, and **6o** were commercially available. The starting materials **6e**,[11b] **6g**,[20] **6i**,[21] **6j**,[22] and **6k**,[22] were prepared according to literature procedures.

General Procedure A for 1,4-Diketone Formation: Freshly distilled styrene (**5**) (2.0 equiv.) and the respective β-dicarbonyl compound **6** (1 mmol, 1.0 equiv.) were added to a suspension of $CeCl_3 \cdot 7H_2O$ (0.05 or 0.1 equiv.) in *i*PrOH (0.65 mL/1 mmol of **6**) and the resulting mixture was stirred at 23 °C. In some cases another portion of styrene (**5**) (1.0 equiv.) was added after 4 h, and the reaction mixture was stirred for a further 20 h at ambient temperature. All volatile materials were removed in vacuo, and the residue was suspended in CH_2Cl_2 (2 ml/mmol of **6**). Pyridine (5.0 equiv.) and ace-

tyl chloride (6.0 equiv.) were added at 0 °C, and the resulting mixture stirred for 16 h at 23 °C. After filtration through a short plug of SiO_2 (PE/EA, 2:1) and evaporation of the solvents the residue was chromatographed on SiO_2 (PE/EA, 5:1) to give the 1,4-diketones **2** as the major products.

Ethyl 2-Oxo-1-(2-oxo-2-phenylethyl)cyclopentane-1-carboxylate (2a): β-Keto ester **6a** (781 mg, 5.00 mmol), $CeCl_3 \cdot 7H_2O$ (185 mg, 0.497 mmol), styrene (**5**) (1.15 mL, 10.0 mmol and 0.58 mL, 5.1 mmol) in *i*PrOH (3.3 mL) and pyridine (2.03 mL, 25.0 mmol), AcCl (2.15 mL, 30.0 mmol) in CH_2Cl_2 (10.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 5:1) furnished 1,4-diketone **2a** [945 mg, 3.45 mmol, 69%, R_f(PE/EA, 2:1) = 0.47] as a colorless oil. $C_{16}H_{18}O_4$ (274.31): calcd. C 70.06, H 6.61; found C 69.57, H 6.62. All spectroscopic data were in accordance with the literature.[10b]

Ethyl 2-Oxo-1-(2-oxo-2-phenylethyl)cyclohexane-1-carboxylate (2b): β-Keto ester **6b** (851 mg, 5.00 mmol), $CeCl_3 \cdot 7H_2O$ (93 mg, 0.25 mmol), styrene (**5**) (1.15 mL, 10.0 mmol and 0.58 mL, 5.1 mmol) in *i*PrOH (3.3 mL) and pyridine (2.03 mL, 25.0 mmol), AcCl (2.15 mL, 30.0 mmol) in CH_2Cl_2 (10.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 10:1) furnished 1,4-diketone **2b** [878 mg, 3.05 mmol, 61% R_f(PE/EA, 2:1) = 0.51] as a colorless solid, m.p. 90 °C. $C_{17}H_{20}O_4$ (288.34): calcd. C 70.81, H 6.99; found C 70.92, H 7.05. All spectroscopic data were in accordance with the literature.[10b]

Methyl 2-Oxo-1-(2-oxo-2-phenylethyl)cycloheptane-1-carboxylate (2c): β-Keto ester **6c** (340 mg, 2.00 mmol), $CeCl_3 \cdot 7H_2O$ (37 mg, 0.10 mmol), styrene (**5**) (0.46 mL, 4.0 mmol and 0.23 mL, 2.0 mmol) in *i*PrOH (1.3 mL) and pyridine (0.81 mL, 10.0 mmol), AcCl (0.86 mL, 12.0 mmol) in CH_2Cl_2 (4.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 5:1) furnished 1,4-diketone **2c** [410 mg, 1.42 mmol, 71%, R_f(PE/EA, 2:1) = 0.45] as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.29–1.37 (m, 1 H), 1.53–1.63 (m, 2 H), 1.69–1.79 (m, 2 H), 1.81–1.91 (m, 1 H), 2.14 (ddd, J = 0.9, J = 9.6, J = 15.2 Hz, 1 H), 2.35 (dd, J = 9.6, J = 15.0 Hz, 1 H), 2.59 (ddd, J = 2.7, J = 8.4, J = 14.5 Hz, 1 H), 2.90 (ddd, J = 2.9, J = 10.5, J = 11.5 Hz, 1 H), 3.29 (d, J = 17.7 Hz, 1 H), 3.74 (s, 3 H), 3.87 (d, J = 17.7 Hz, 1 H), 7.43–7.48 (m, 2 H), 7.53–7.58 (m, 1 H), 7.95–7.97 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 25.11 (CH_2), 26.34 (CH_2), 31.87 (CH_2), 34.56 (CH_2), 41.39 (CH_2), 43.21 (CH_2), 54.03 (CH_3), 61.59 (C), 128.07 (CH), 128.58 (CH), 133.20 (CH), 136.77 (C), 172.49 (C), 197.33 (C), 209.02 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2939 (m), 1733 (vs), 1706 (vs), 1686 (vs), 1448 (m), 1219 (m), 1201 (m), 1167 (m), 1154 (m) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 288 (1) [M$^+$], 270 (4), 256 (30), 168 (38), 137 (18), 120 (17), 105 (100), 77 (38). $C_{17}H_{20}O_4$ (288.34): calcd. C 70.81, H 6.99; found C 70.74, H 7.01.

2-Acetyl-2-(2-oxo-2-phenylethyl)-4-butanolide (2d): Lactone **6d** (110 mg, 0.859 mmol), $CeCl_3 \cdot 7H_2O$ (15 mg, 0.040 mmol), styrene (**5**) (176 mg, 1.69 mmol) in *i*PrOH (0.25 mL) and pyridine (0.36 mL, 4.35 mmol), AcCl (0.37 mL, 5.22 mmol) in CH_2Cl_2 (1.7 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 2:1) furnished 1,4-diketone **2d** (184 mg, 0.747 mmol, 87%) as a yellowish oil. All spectroscopic data were in accordance with the literature.[10b]

3-Acetyl-1-benzyl-3-(2-oxo-2-phenylethyl)pyrrolidin-2-one (2e): Lactam **6e** (1.09 g, 5.00 mmol), $CeCl_3 \cdot 7H_2O$ (185 mg, 0.497 mmol), styrene (**5**) (1.15 mL, 10.0 mmol and 0.58 mL, 5.1 mmol) in *i*PrOH (3.3 mL) and pyridine (2.03 mL, 25.0 mmol), AcCl (2.15 mL, 30.0 mmol) in CH_2Cl_2 (10.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 2:1) furnished 1,4-diketone **2e** [1.21 g, 3.60 mmol, 72%, R_f(PE/EA, 2:1) = 0.21] as a colorless oil. All spectroscopic data were in accordance with the literature.[10b]

2-Acetyl-2-(2-oxo-2-phenylethyl)cyclopentanone (2f): Diketone **6f** (625 mg, 4.95 mmol), $CeCl_3 \cdot 7H_2O$ (93 mg, 0.25 mmol), styrene (**5**) (1.15 mL, 10.0 mmol and 0.58 mL, 5.1 mmol) in *i*PrOH (3.3 mL) and pyridine (2.03 mL, 25.0 mmol), AcCl (2.15 mL, 30.0 mmol) in CH_2Cl_2 (10.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 5:1) furnished 1,4-diketone **2f** [740 mg, 3.03 mmol, 61%, R_f(PE/EA, 2:1) = 0.40] as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.85–1.95 (m, 1 H), 2.02–2.08 (m, 2 H), 2.21 (s, 3 H), 2.36–2.48 (m, 1 H), 2.52–2.60 (m, 1 H), 2.84 (dt, J = 5.0, J = 13.5 Hz, 1 H), 3.50 (d, J = 18.5 Hz, 1 H), 3.80 (d, J = 18.5 Hz, 1 H), 7.45–7.49 (m, 2 H), 7.57–7.61 (m, 1 H), 7.92–7.94 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 62 MHz): δ = 19.71 (CH_2), 26.37 (CH_3), 31.94 (CH_2), 38.13 (CH_2), 44.47 (CH_2), 65.70 (C), 128.08 (CH), 128.76 (CH), 133.70 (CH), 136.14 (C), 196.57 (C), 202.77 (C), 215.61 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1736 (vs), 1700 (vs), 1680 (vs), 1351 (m), 1219 (m), 1155 (m), 1105 (m) cm^{-1}. HRMS (70 eV, EI): calcd. 244.1099 (for $C_{15}H_{16}O_3$), found 244.1099 [M$^+$]. $C_{15}H_{16}O_3$ (244.28): calcd. C 73.75, H 6.60; found C 73.71, H 6.80.

2-Acetyl-2-(2-oxo-2-phenylethyl)cycloheptanone (2g): Diketone **6g** (308 mg, 2.00 mmol), $CeCl_3 \cdot 7H_2O$ (74 mg, 0.20 mmol), styrene (**5**) (0.46 mL, 4.0 mmol and 0.23 mL, 2.0 mmol) in *i*PrOH (1.3 mL) and pyridine (0.81 mL, 10.0 mmol), AcCl (0.86 mL, 12.0 mmol) in CH_2Cl_2 (4.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 5:1) furnished 1,4-diketone **2g** [74 mg, 0.27 mmol, 14%, R_f(PE/EA, 2:1) = 0.43] as a colorless solid, which contained single crystals suitable for X-ray structure analysis. M.p. 85 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.13–1.21 (m, 1 H), 1.41–1.54 (m, 3 H), 1.78–1.83 (m, 2 H), 1.98 (dd, J = 8.8, J = 15.3 Hz, 1 H), 2.17 (s, 3 H), 2.43–3.48 (m, 2 H), 2.78 (dt, J = 2.6, J = 11.7 Hz, 1 H), 3.34 (d, J = 18.3 Hz, 1 H), 4.02 (dd, J = 0.9, J = 18.3 Hz, 1 H), 7.46–7.49 (m, 2 H), 7.57–7.60 (m, 1 H), 7.97–7.99 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 24.49 (CH_2), 26.56 (CH_3), 26.78 (CH_2), 30.38 (CH_2), 30.93 (CH_2), 41.17 (CH_2), 43.29 (CH_2), 69.24 (C), 128.15 (CH), 128.69 (CH), 133.46 (CH), 136.56 (C), 197.66 (C), 204.92 (C), 210.64 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2929 (m), 2862 (m), 1742 (m), 1703 (s), 1692 (vs), 1677 (vs), 1596 (m), 1579 (m), 1445 (s), 1361 (s), 1342 (s), 1180 (m), 1156 (vs), 1035 (m), 882 (m), 817 (m) cm^{-1}. HRMS (CI, CH_4): calcd. 273.1481 (for $C_{17}H_{21}O_3$), found 273.1472 [MH$^+$].

Methyl 2-Acetyl-4-oxo-4-phenylbutyrate (2h): β-Keto ester **6h** (232 mg, 2.00 mmol), $CeCl_3 \cdot 7H_2O$ (75 mg, 0.20 mmol), styrene (**5**) (0.46 mL, 4.0 mmol and 0.23 mL, 2.0 mmol) in *i*PrOH (1.3 mL) and pyridine (0.81 mL, 10.0 mmol), AcCl (0.87 mL, 12.0 mmol) in CH_2Cl_2 (4.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 5:1) furnished 1,4-diketone **2h** [338 mg, 1.44 mmol, 72%, R_f(PE/EA, 2:1) = 0.44] as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.44 (s, 3 H), 3.54 (dd, J = 5.4, J = 18.3 Hz, 1 H), 3.73 (dd, J = 8.3, J = 18.4 Hz, 1 H), 3.78 (s, 3 H), 4.24 (dd, J = 5.6, J = 8.2 Hz, 1 H), 7.45–7.49 (m, 2 H), 7.55–7.60 (m, 1 H), 7.95–7.99 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 30.29 (CH_3), 37.48 (CH_2), 52.75 (CH), 53.67 (CH_3), 128.14 (CH), 128.65 (CH), 133.54 (CH), 136.06 (C), 169.44 (C), 197.08 (C), 202.25 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1742 (s), 1717 (s), 1685 (s), 1597 (m), 1449 (m), 1435 (m), 1353 (m), 1265 (s), 1170 (s), 1069 (m), 1001 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 234 (1) [M$^+$], 216 (2), 203 (7), 192 (37), 174 (14), 105 (100), 87 (37),

77 (27), 43 (35). $C_{13}H_{14}O_4$ (234.25): calcd. C 66.66, H 6.02; found C 66.41, H 6.02.

Ethyl 2-Acetyl-2-methyl-4-oxo-4-phenylbutyrate (2i): β-Keto ester **6i** (288 mg, 2.00 mmol), $CeCl_3 \cdot 7H_2O$ (75 mg, 0.20 mmol), styrene (**5**) (0.46 mL, 4.0 mmol and 0.23 mL, 2.0 mmol) in *i*PrOH (1.3 mL) and pyridine (0.81 mL, 10.0 mmol), AcCl (0.87 mL, 12.0 mmol) in CH_2Cl_2 (4.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 2:1) furnished 1,4-diketone **2i** [356 mg, 1.36 mmol, 68%, R_f(PE/EA, 2:1) = 0.50] as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.24 (t, J = 7.2 Hz, 3 H), 1.57 (s, 3 H), 2.34 (s, 3 H), 3.62 (d, J = 18.2 Hz, 1 H), 3.68 (d, J = 18.2 Hz, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 7.44–7.48 (m, 2 H), 7.55–7.59 (m, 1 H), 7.95–7.98 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 13.98 (CH_3), 20.76 (CH_3), 26.47 (CH_3), 44.64 (CH_2), 57.35 (C), 61.61 (CH_2), 128.09 (CH), 128.65 (CH), 133.37 (CH), 136.67 (C), 162.49 (C), 172.37 (C), 197.12 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2982 (m), 1735 (s), 1714 (vs), 1688 (s), 1449 (m), 1355 (m), 1226 (m), 1186 (m), 1101 (m) cm^{-1}. HRMS (CI, CH_4): calcd. 263.1283 (for $C_{15}H_{19}O_4$), found 263.1275 [MH^+].

Ethyl 2-Acetyl-2-ethyl-4-oxo-4-phenylbutyrate (2j): β-Keto ester **6j** (790 mg, 5.00 mmol), $CeCl_3 \cdot 7H_2O$ (186 mg, 0.497 mmol), styrene (**5**) (1.15 mL, 10.0 mmol and 0.58 mL, 5.1 mmol) in *i*PrOH (3.3 mL) and pyridine (2.03 mL, 25.0 mmol), AcCl (2.13 mL, 30.0 mmol) in CH_2Cl_2 (10.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 10:1) furnished 1,4-diketone **2j** [575 mg, 2.08 mmol, 42%, R_f(PE/EA, 2:1) = 0.62] as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.84 (t, J = 7.6 Hz, 3 H), 1.23 (t, J = 7.0 Hz, 3 H), 2.09 (qd, J = 7.6, J = 15.0 Hz, 1 H), 2.18 (qd, J = 7.7, J = 15.3 Hz, 1 H), 2.37 (s, 3 H), 3.63 (d, J = 18.5 Hz, 1 H), 3.68 (d, J = 18.5 Hz, 1 H), 4.20 (q, J = 7.0 Hz, 2 H), 7.44–7.48 (m, 2 H), 7.55–7.59 (m, 1 H), 7.96–7.98 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 9.00 (CH_3), 14.00 (CH_3), 26.90 (CH_2), 27.31 (CH_3) 41.19 (CH_2), 61.40 (CH_2), 61.69 (C), 128.07 (CH), 128.62 (CH), 133.30 (CH), 136.58 (C), 171.94 (C), 197.46 (C), 205.73 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2977 (m), 1729 (s), 1710 (vs), 1684 (vs), 1597 (m), 1581 (m), 1448 (s), 1354 (s), 1218 (vs), 1180 (vs), 1101 (m), 1017 (m) cm^{-1}. MS (CI, CH_4): *m*/*z* (%) = 277 (45) [MH^+], 259 (84), 234 (60), 231 (100), 216 (5), 187 (59), 159 (14), 129 (21), 105 (66), 101 (15), 77 (18). $C_{16}H_{20}O_4$ (276.33): calcd. C 69.55, H 7.30; found C 69.57, H 7.40.

Ethyl 2-Acetyl-2-benzyl-4-oxo-4-phenylbutyrate (2k): β-Keto ester **6k** (440 mg, 2.00 mmol), $CeCl_3 \cdot 7H_2O$ (74 mg, 0.497 mmol), styrene (**5**) (0.46 mL, 4.0 mmol and 0.23 mL, 2.0 mmol) in *i*PrOH (1.3 mL) and pyridine (0.81 mL, 10.0 mmol), AcCl (0.86 mL, 12.0 mmol) in CH_2Cl_2 (4.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 10:1) furnished 1,4-diketone **2k** [360 mg, 1.06 mmol, 53%, R_f(PE/EA, 2:1) = 0.59] as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.23 (t, J = 7.1 Hz, 3 H), 2.46 (s, 3 H), 3.35 (d, J = 13.9 Hz 1 H), 3.50 (d, J = 18.5 Hz, 1 H), 3.56 (d, J = 13.9 Hz, 1 H), 3.57 (d, J = 18.5 Hz, 1 H), 4.20 (q, J = 7.1 Hz, 2 H), 6.94–6.96 (m, 2 H), 7.19–7.21 (m, 3 H), 7.42–7.45 (m, 2 H), 7.55–7.57 (m, 1 H), 7.87–7.89 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 13.95 (CH_3), 27.51 (CH_3), 39.29 (CH_2), 41.87 (CH_2), 61.64 (CH_2), 62.33 (C), 127.15 (CH), 128.05 (2 CH), 128.48 (CH), 128.60 (CH), 129.77 (CH), 133.39 (CH), 136.06 (C), 136.38 (C), 171.26 (C), 197.75 (C), 205.03 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1711 (vs), 1683 (vs), 1597 (m), 1495 (m), 1448 (m), 1354 (s), 1267 (m), 1219 (s), 1181 (vs), 1082 (m), 1003 (m), 861 (m), 745 (s) cm^{-1}. HRMS (CI, CH_4): calcd. 338.1518 (for $C_{21}H_{22}O_4$), found 338.1514 [M^+]; calcd. 339.1596 (for $C_{21}H_{23}O_4$), found 339.1579 [MH^+].

Ethyl 2-Benzoyl-4-oxo-4-phenylbutyrate (2l): β-Keto ester **6l** (358 mg, 1.86 mmol), $CeCl_3 \cdot 7H_2O$ (74 mg, 0.20 mmol), styrene (**5**) (0.46 mL, 4.0 mmol and 0.23 mL, 2.0 mmol) in *i*PrOH (1.3 mL) and pyridine (0.81 mL, 10.0 mmol), AcCl (0.86 mL, 12.0 mmol) in CH_2Cl_2 (4.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 10:1) furnished 1,4-diketone **2l** [323 mg, 1.04 mmol, 56%, R_f(PE/EA, 2:1) = 0.55] as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.17 (t, J = 7.1 Hz, 3 H), 3.73 (dd, J = 6.0, J = 18.1 Hz, 1 H), 3.82 (dd, J = 7.6, J = 18.1 Hz, 1 H), 4.16 (q, J = 7.2 Hz, 2 H), 5.12 (dd, J = 6.1, J = 7.5 Hz, 1 H), 7.45–7.52 (m, 4 H), 7.56–7.62 (m, 2 H), 7.99–8.01 (m, 2 H), 8.09–8.10 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 62 MHz): δ = 13.85 (CH_3), 38.17 (CH_2), 48.87 (CH), 61.79 (CH_2), 128.23 (CH), 128.67 (CH), 128.71 (CH), 128.97 (CH), 133.52 (CH), 133.58 (CH), 136.11 (2 C), 169.38 (C), 194.82 (C), 196.91 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1732 (s), 1678 (vs), 1596 (m), 1580 (m), 1448 (m), 1329 (m), 1270 (m), 1243 (m), 1216 (s), 1181 (m), 1001 (m) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 310 (0.2) [M^+], 292 (0.3), 265 (2), 233 (2), 205 (2), 188 (13), 105 (100), 77 (18). $C_{19}H_{18}O_4$ (310.35): calcd. C 73.53, H 5.85; found C 73.54, H 5.98.

3-Acetyl-1-phenylpentane-1,4-dione (2m): Acetylacetone (**6m**) (200 mg, 2.00 mmol), $CeCl_3 \cdot 7H_2O$ (74 mg, 0.20 mmol), styrene (**5**) (0.46 mL, 4.0 mmol and 0.23 mL, 2.0 mmol) in *i*PrOH (1.3 mL) and pyridine (0.81 mL, 10.0 mmol), AcCl (0.86 mL, 12.0 mmol) in CH_2Cl_2 (4.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 5:1) furnished 1,4-diketone **2m** [123 mg, 0.564 mmol, 28%, R_f(PE/EA, 2:1) = 0.22] as a yellowish oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.36 (s, 6 H), 3.59 (d, J = 6.9 Hz, 2 H), 4.39 (t, J = 6.9 Hz, 1 H), 7.45–7.49 (m, 2 H), 7.57–7.60 (m, 1 H), 7.95–7.98 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 30.01 (CH_3), 37.77 (CH_2), 52.67 (C), 62.59 (CH), 128.16 (CH), 128.73 (CH), 133.63 (CH), 136.02 (C), 162.46 (C), 196.97 (C), 202.99 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1726 (m), 1700 (s), 1681 (vs), 1596 (m), 1580 (m), 1448 (m), 1419 (m), 1356 (s), 1254 (m), 1212 (s), 1156 (s), 1001 (m) cm^{-1}. MS (CI, CH_4): *m*/*z* (%) = 219 (100) [MH^+], 201 (79), 177 (12), 158 (49), 105 (30), 77 (5). $C_{13}H_{14}O_3$ (218.25): calcd. C 71.54, H 6.47; found C 71.22, H 6.46.

3-Acetyl-3-methyl-1-phenylpentane-1,4-dione (2n): β-Diketone **6n** (228 mg, 2.00 mmol), $CeCl_3 \cdot 7H_2O$ (74 mg, 0.20 mmol), styrene (**5**) (0.46 mL, 4.0 mmol and 0.23 mL, 2.0 mmol) in *i*PrOH (1.3 mL) and pyridine (0.81 mL, 10.0 mmol), AcCl (0.86 mL, 12.0 mmol) in CH_2Cl_2 (4.0 mL) were converted according to the General Procedure A. Chromatography (SiO_2, PE/EA, 5:1) furnished 1,4-diketone **2n** [46 mg, 0.198 mmol, 10%, R_f(PE/EA, 2:1) = 0.31] as a colorless solid. M.p. 59 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.56 (s, 3 H), 2.22 (s, 6 H), 3.71 (s, 2 H), 7.47–7.50 (m, 2 H), 7.56–7.60 (m, 1 H), 7.95–7.99 (m, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 62 MHz): δ = 19.60 (CH_3), 26.50 (CH_3), 44.85 (CH_2), 64.54 (C), 128.14 (CH), 128.73 (CH), 133.60 (CH), 136.44 (C), 197.28 (C), 206.21 (C) ppm. IR (ATR): $\tilde{\nu}$ = 1740 (m), 1694 (vs), 1683 (s), 1595 (m), 1579 (m), 1448 (m), 1368 (s), 1353 (s), 1215 (s), 1169 (s), 1092 (m), 1015 (m) cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 233 (0.3) [MH^+], 214 (1), 190 (8), 172 (45), 147 (5), 105 (100), 85 (68), 77 (25), 57 (7). $C_{14}H_{16}O_3$ (232.28): calcd. C 72.39, H 6.94; found C 72.26, H 7.00.

General Procedure B for 3-Hydroxy-1,2-dioxane Formation: The β-dicarbonyl compound **6** (1.0 equiv.) was added to a suspension of $CeCl_3 \cdot 7H_2O$ (0.05 equiv.) and styrene (**5**) (2.0 equiv.) in *i*PrOH. After stirring the mixture for 14–16 h under an atmosphere of air and at ambient temperature, all volatile materials were removed in vacuo and the residue purified by chromatography on SiO_2 (PE/EA).

6-Hydroxy-6-methyl-9-phenyl-7,8-dioxaspiro[4.5]decan-1-one (1a) and 6-Acetyl-1-hydroxy-4-phenyl-2,3-dioxabicyclo[4.3.0]nonan-1-on (1c): $CeCl_3 \cdot 7H_2O$ (30 mg, 0.081 mmol), styrene (**5**) (338 mg,

3.25 mmol) and β-diketone **6f** (197 mg, 1.56 mmol) were converted in 0.5 mL *i*PrOH according to the General Procedure B. Chromatography (SiO_2, PE/EA, 5:1) gave a first fraction with a mixture of the title compounds **1a** and **1c** [90 mg, 0.34 mmol, 22%, **1a/1c** 75:25, R_f(SiO_2, PE/EA, 2:1) = 0.22] as a colorless solid, m.p. 102–105 °C. The second fraction contained the 1,4-diketone **2f** (34 mg, 0.14 mmol, 9%) as yellowish oil. ^{1}H NMR (500 MHz, $CDCl_3$), isomer **1a** und **1c**: δ = 1.34 (s, 3 H, CH_3, isomer **1a**), 1.75–1.88 (m, 4 H), 1.89–1.95 (m, 2 H), 1.96–2.01 (m, 2 H), 2.08–2.15 (m, 1 H), 2.16–2.22 (m, 1 H), 2.21–2.37 (m, 4 H), 2.29 (s, 3 H, CH_3, isomer **1c**), 2.46–2.52 (m, 2 H), 3.54 (br. s, 1 H, OH, isomer **1c**), 4.28 (br. s, 1 H, OH, isomer **1c**), 5.31 (dd, J = 11.4, J = 2.5 Hz, 1 H, CH, isomer **1c**), 5.57 (dd, J = 11.7, J = 2.2 Hz, 1 H, CH, isomer **1a**), 7.31–7.38 (m, 10 H, CH) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$), isomer **1a**: δ = 18.12 (CH_2), 20.86 (CH_3), 34.52 (CH_2), 34.93 (CH_2), 39.57 (CH_2), 52.26 (C), 78.45 (CH), 100.21 (C), 127.14 (CH), 128.64 (CH), 128.92 (CH), 137.30 (C), 217.94 (C=O) ppm. Isomer **1c**. δ = 19.03 (CH_2), 27.17 (CH_3), 30.58 (CH_2), 33.07 (CH_2), 35.36 (CH_2), 57.44 (C), 77.26 (CH), 108.17 (C), 126.97 (CH), 128.60 (CH), 128.68 (CH), 137.57 (C), 211.67 (C=O) ppm. MS (FAB, glycerol): *m/z* (%) = 263 (9) [MH^+], 245 (100) [$M^+ - H_2O$], 229 (84) [$M^+ - H_2O_2$], 203 (13), 187 (15), 151 (34), 105 (12). IR (ATR): $\tilde{\nu}$ = 3385 (br. s), 1729 (vs), 1670 (vs), 1453 (m), 1376 (m), 1320 (m), 1272 (m), 1156 (s) cm^{-1}. HRMS (CI, CH_4): calcd. 263.1283 (for $C_{15}H_{19}O_4$), found 263.1280 [MH^+].

7-Hydroxy-7-methyl-10-phenyl-8,9-dioxaspiro[5.5]undecane-1-one (1b): $CeCl_3 \cdot 7H_2O$ (30 mg, 0.081 mmol), styrene (**5**) (333 mg, 3.20 mmol) and β-diketone **6o** (226 mg, 1.55 mmol) were converted in 0.5 mL *i*PrOH according to the General Procedure B. Chromatography (SiO_2, PE/EA, 5:1) gave the title compound **1b** as a mixture of diastereoisomers A and B [140 mg, 0.507 mmol, 33%; A/B = 71:29, isomer A: R_f(SiO_2, PE/EA, 2:1) = 0.38, isomer B: R_f(SiO_2, PE/EA, 2:1) = 0.42] as a colorless oil. Both isomers could be separated by repeated chromatography. Isomer A: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26 (qt, J = 13.6, J = 1.5 Hz, 1 H), 1.50 (qt, J = 13.5, J = 4.1 Hz, 1 H), 1.59–1.65 (m, 1 H), 1.66–1.72 (m, 1 H), 1.75–1.81 (m, 1 H), 1.84–1.88 (m, 1 H), 1.90–1.95 (m, 1 H), 2.11 (dt, J = 14.1, J = 5.1 Hz, 1 H), 2.22 (s, 3 H, CH_3), 2.38 (dt, J = 14.0, J = 3.6 Hz, 1 H), 2.51 (dd, J = 13.2, J = 11.8 Hz, 1 H), 4.22 (br. s, 1 H, OH), 5.46 (dd, J = 11.7, J = 2.5 Hz, 1 H, CH), 7.32–7.39 (m, 5 H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 22.24 (CH_2), 22.79 (CH_2), 26.14 (CH_3), 30.36 (CH_2), 34.58 (CH_2), 36.02 (CH_2), 53.38 (C), 78.22 (CH), 99.54 (C), 127.10 (CH), 128.68 (CH), 129.01 (CH), 137.59 (C), 212.51 (C=O) ppm. Isomer B: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.60–1.74 (m, 4 H), 1.75–1.80 (m, 2 H), 1.87 (dq, J = 13.1, J = 4.6 Hz, 1 H), 2.25–2.29 (m, 1 H), 2.32 (s, 3 H, CH_3), 2.41–2.54 (m, 1 H), 2.74 (dd, J = 14.7, J = 12.2 Hz, 1 H), 5.05 (dd, J = 12.0, J = 2.1 Hz, 1 H, CH), 7.16 (br. s, 1 H, OH), 7.33–7.42 (m, 5 H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 20.36 (CH_2), 22.54 (CH_2), 26.84 (CH_3), 31.32 (CH_2), 32.38 (CH_2), 36.07 (CH_2), 52.36 (C), 81.21 (CH), 104.19 (C), 126.75 (CH), 128.76 (CH), 129.00 (CH), 137.84 (C), 217.01 (C=O) ppm. MS (FAB, glycerol): *m/z* (%) = 277 (26) [MH^+], 259 (100) [$MH^+ - H_2O$], 243 (93) [$MH^+ - H_2O_2$], 217 (16), 199 (20), 165 (29), 132 (56), 123 (40), 105 (26). IR (ATR): $\tilde{\nu}$ = 3322 (br. m), 2940 (s), 2868 (m), 1685 (s), 1453 (s) cm^{-1}. $C_{16}H_{20}O_4$ (276.14): calcd. C 69.55, H 7.30; found C 69.66, H 7.28.

Ethyl 4-Ethyl-3-hydroxy-3-methyl-6-phenyl-1,2-dioxane-4-carboxylate (1d): $CeCl_3 \cdot 7H_2O$ (30 mg, 0.081 mmol), styrene (**5**) (333 mg, 3.20 mmol) and β-keto ester **6j** (261 mg, 1.65 mmol) were converted in 0.5 mL *i*PrOH according to the General Procedure B. Chromatography (SiO_2, PE/EA, 10:1) gave two fractions with the product. In the first a mixture of two diastereoisomers A and B [36 mg, 0.12 mmol, 7%, A/B = 53:47, R_f(SiO_2, PE/EA, 5:1) = 0.28] was obtained as a colorless oil. The second fraction contained a third isomer C [49 mg, 0.17 mmol, 11%, R_f(SiO_2, PE/EA, 5:1) = 0.20] as colorless crystals. Single crystals were grown from isomer C. Isomers A and B: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.82 (t, J = 7.6 Hz, 3 H, CH_3, isomer B), 0.92 (t, J = 7.5 Hz, 3 H, CH_3, isomer A), 1.33 (t, J = 7.2 Hz, 3 H, CH_3, isomer B), 1.38 (t, J = 7.2 Hz, 3 H, CH_3, isomer A), 1.53 (s, 3 H, CH_3, isomer B), 1.55–1.61 (m, 1 H), 1.66–1.73 (m, 1 H), 1.70 (s, 3 H, CH_3, isomer A), 1.92–2.02 (m, 3 H), 2.05–2.12 (m, 1 H), 2.39 (dd, J = 14.0, J = 2.5 Hz, 1 H, isomer B), 2.69 (dd, J = 14.1, J = 2.5 Hz, 1 H, isomer A), 3.53 (s, 1 H, OH, isomer B), 4.21–4.29 (m, 2 H, OCH_2, isomer B), 4.29–4.42 (m, 2 H, OCH_2, isomer A), 5.21 (dd, J = 11.7, J = 2.4 Hz, 1 H, CH, isomer A), 5.76 (dd, J = 11.6, J = 2.5 Hz, 1 H, CH, isomer B), 7.17 (br. s, 1 H, OH, isomer A), 7.31–7.39 (m, 10 H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$), isomer A: δ = 8.87 (CH_3), 14.18 (CH_3), 22.05 (CH_3), 28.20 (CH_2), 34.19 (CH_2), 52.85 (C), 61.94 (CH_2), 81.19 (CH), 101.63 (C), 126.78 (CH), 128.65 (CH), 128.81 (CH), 138.14 (C), 176.34 (C=O) ppm. Isomer B: δ = 8.21 (CH_3), 14.18 (CH_3), 20.36 (CH_3), 28.90 (CH_2), 34.19 (CH_2), 52.51 (C), 60.95 (CH_2), 81.64 (CH), 104.53 (C), 126.96 (CH), 128.65 (CH), 128.76 (CH), 137.49 (C), 172.98 (C=O) ppm. MS (EI, 70 eV): *m/z* (%) = 294 (2) [M^+], 276 (3) [$M^+ - H_2O$], 262 (12) [$M^+ - O_2$], 234 (19), 190 (8), 188 (29), 158 (53), 143 (19), 129 (32), 105 (100), 77 (51). IR (ATR): $\tilde{\nu}$ = 3352 (br. m), 2976 (s), 2942 (m), 1724 (vs), 1694 (vs), 1455 (s), 1371 (m), 1312 (m), 1234 (m), 1215 (s), 1196 (s), 1124 (m), 1036 (m) cm^{-1}. $C_{16}H_{22}O_5$ (294.34): calcd. C 65.29, H 7.53; found C 65.46, H 7.56. Isomer C: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.87 (t, J = 7.5 Hz, 3 H, CH_3), 1.29 (t, J = 7.1 Hz, 3 H, CH_3), 1.58 (s, 3 H, CH_3), 1.99–2.06 (m, 1 H), 2.06–2.15 (m, 2 H), 2.73 (ddd, J = 14.8, J = 12.3, J = 1.3 Hz, 1 H), 3.50 (br. s, 1 H, OH), 4.15–4.27 (m, 2 H, CH_2), 5.18 (dd, J = 12.3, J = 2.0 Hz, 1 H, CH), 7.33–7.42 (m, 5 H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 9.02 (CH_3), 14.18 (CH_3), 20.94 (CH_3), 23.70 (CH_2), 29.65 (CH_2), 52.17 (C), 61.16 (CH_2), 78.83 (CH), 102.12 (C), 127.16 (CH), 128.64 (CH), 128.96 (CH), 137.40 (C), 173.02 (C=O) ppm. M.p. 89–92 °C. $C_{16}H_{22}O_5$ (294.34): calcd. C 65.29, H 7.53; found C 65.59, H 7.50.

Ethyl 6-Hydroxy-3-phenyl-4,5-dioxabicyclo[4.4.0]decane-1-carboxylate (1e): $CeCl_3 \cdot 7H_2O$ (30 mg, 0.081 mmol), styrene (**5**) (331 mg, 3.18 mmol) and β-keto ester **6b** (267 mg, 1.57 mmol) were converted in 0.5 mL *i*PrOH according to the General Procedure B. Chromatography (SiO_2, PE/EA, 10:1) gave a mixture of two diastereoisomers A and B (240 mg, 0.785 mmol, 50%, A/B = 50:50), which were separated by repeated chromatography [isomer A: R_f(SiO_2, PE/EA, 5:1) = 0.32; isomer B: R_f(SiO_2, PE/EA, 5:1) = 0.15]. Single crystals were grown from isomer A, m.p. 118 °C. $C_{17}H_{22}O_5$ (306.15): calcd. C 66.65, H 7.24; found C 66.79, H 7.15. All spectroscopic data were in accordance with the literature.[10b]

Methyl 7-Hydroxy-10-methyl-10-phenyl-8,9-dioxabicyclo[5.4.0]undecane-1-carboxylate (1f): $CeCl_3 \cdot 7H_2O$ (30 mg, 0.081 mmol), α-methylstyrene (393 mg, 3.33 mmol) and β-keto ester **6c** (291 mg, 1.71 mmol) were converted in 0.5 mL *i*PrOH according to the General Procedure B. Chromatography (SiO_2, PE/EA, 10:1) gave a mixture of four diastereoisomers A, B, C, and D (288 mg, 0.899 mmol, 53%, A/B/C/D = 38:25:24:16), which were partly separated by repeated chromatography [isomer A and D: R_f(SiO_2, PE/EA, 5:1) = 0.28; isomer B and C: R_f(SiO_2, PE/EA, 5:1) = 0.34–0.44]. Single crystals of isomer C were grown from a mixture with isomer B, m.p. 124–129 °C. $C_{18}H_{24}O_5$ (320.38): calcd. C 67.48, H 7.55; found C 67.28, H 7.55. All spectroscopic data were in accordance with the literature.[10b]

Acknowledgments

We acknowledge the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie (fellowship for M. R.) for generous support of this work.

[1] N. Kornblum, H. E. DeLaMare, *J. Am. Chem. Soc.* **1951**, *73*, 880–881.
[2] a) B. W. Greatrex, D. K. Taylor, E. R. T. Tiekink, *J. Org. Chem.* **2004**, *69*, 2580–2583; b) B. W. Greatrex, N. F. Jenkins, D. K. Taylor, E. R. T. Tiekink, *J. Org. Chem.* **2003**, *68*, 5205–5210; c) G. Özer, N. Saracoglu, M. Balci, *J. Org. Chem.* **2003**, *68*, 7009–7015.
[3] D. R. Kelly, H. Bansal, J. J. G. Morgan, *Tetrahedron Lett.* **2002**, *43*, 9331–9333.
[4] Selection of other new 1,4-diketone syntheses: a) M. Yuguchi, M. Tokuda, K. Orito, *J. Org. Chem.* **2004**, *69*, 908–914; b) R. Ballini, L. Barboni, G. Giarlo, *J. Org. Chem.* **2003**, *68*, 9173–9176; c) Y. Yamamoto, H. Maekawa, S. Goda, I. Nishiguchi, *Org. Lett.* **2003**, *5*, 2755–2758; d) M. Yasuda, S. Tsuji, Y. Shigeyoshi, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 7440–7447.
[5] a) B. K. Banik, S. Samajdar, I. Banik, *J. Org. Chem.* **2004**, *69*, 213–216; b) G. Minetto, L. F. Raveglia, M. Taddei, *Org. Lett.* **2004**, *6*, 389–392; c) R. Dhawan, B. A. Arndtsen, *J. Am. Chem. Soc.* **2004**, *126*, 468–469; d) H. S. P. Rao, S. Jothilingam, *J. Org. Chem.* **2003**, *68*, 5392–5394; e) B. W. Greatrex, M. C. Kimber, D. K. Taylor, E. R. T. Tiekink, *J. Org. Chem.* **2003**, *68*, 4239–4246; f) D. S. Mortensen, A. L. Rodriguez, K. E. Carlson, J. Sun, B. S. Katzenellenbogen, J. A. Katzenellenbogen, *J. Med. Chem.* **2001**, *44*, 3838–3848; g) R. U. Braun, K. Zeitler, T. J. J. Müller, *Org. Lett.* **2001**, *3*, 3297–3300.
[6] a) J. Christoffers, in: *Encyclopedia of Catalysis*, vol. 5 (Ed.: I. Horvath), Wiley, New York, **2003**, pp. 99–118; b) N. Krause, A. Hoffmann-Röder, *Synthesis* **2001**, 171–196; c) B. E. Rossiter, N. M. Swingle, *Chem. Rev.* **1992**, *92*, 771–806.
[7] Recent examples: a) M. A. Calter, C. Zhu, *Org. Lett.* **2002**, *4*, 205–208; b) M. A. Calter, C. Zhu, R. J. Lachicotte, *Org. Lett.* **2002**, *4*, 209–212; c) F. Stauffer, R. Neier, *Org. Lett.* **2000**, *2*, 3535–3537.
[8] Review: A. B. Smith III, C. M. Adams, *Acc. Chem. Res.* **2004**, *37*, 365–377.
[9] Review: D. Enders, T. Balensiefer, *Acc. Chem. Res.* **2004**, *37*, 534–541.
[10] a) M. Rössle, T. Werner, A. Baro, W. Frey, J. Christoffers, *Angew. Chem.* **2004**, *116*, 6709–6711; *Angew. Chem. Int. Ed.* **2004**, *43*, 6547–6549; b) J. Christoffers, T. Werner, W. Frey, A. Baro, *Eur. J. Org. Chem.* **2003**, 4879–4886.
[11] a) J. Christoffers, T. Werner, *Synlett* **2002**, 119–121; b) J. Christoffers, T. Werner, S. Unger, W. Frey, *Eur. J. Org. Chem.* **2003**, 425–431; c) J. Christoffers, T. Werner, W. Frey, A. Baro, *Chem. Eur. J.* **2004**, *10*, 1042–1045; d) Review: J. Christoffers, A. Baro, T. Werner, *Adv. Synth. Catal.* **2004**, *346*, 143–151.
[12] At least to some extend 1,4-diketones might already form by direct oxidation of the benzyl radical by Ce^{IV} species as was observed earlier by us in certain cases.[10b] See also: a) V. Nair, J. Mathew, *J. Chem. Soc., Perkin Trans. 1* **1995**, 1881–1882; b) Review: V. Nair, L. Balagopal, R. Rajan, J. Mathew, *Acc. Chem. Res.* **2004**, *37*, 21–30.
[13] a) E. Camacho, J. Leon, A. Carrion, A. Entrena, G. Escames, H. Khaldy, D. Acuna-Castroviejo, M. A. Gallo, A. Espinosa, *J. Med. Chem.* **2002**, *45*, 263–274; b) M. Van der Mey, A. Hatzelmann, I. J. Van der Laan, G. J. Sterk, U. Thibaut, H. Timmerman, *J. Med. Chem.* **2001**, *44*, 2511–2522; c) M. Yasuda, S. Tsuji, I. Shibata, A. Baba, *J. Org. Chem.* **1997**, *62*, 8282–8283; d) F. Ros, J. de la Rosa, J. Enfedaque, *J. Org. Chem.* **1995**, *60*, 5419–5424; e) F. F. Owings, M. Fox, C. J. Kowalski, N. H. Baine, *J. Org. Chem.* **1991**, *56*, 1963–1966.
[14] a) J.-Q. Yu, E. J. Corey, *J. Am. Chem. Soc.* **2003**, *125*, 3232–3233; b) B. Greatrex, M. Jevric, M. C. Kimber, S. J. Krivickas, D. K. Taylor, E. R. T. Tiekink, *Synthesis* **2003**, 668–672; c) B. W. Greatrex, M. C. Kimber, D. K. Taylor, G. Fallon, E. R. T. Tiekink, *J. Org. Chem.* **2002**, *67*, 5307–5314; d) M. C. Kimber, D. K. Taylor, *J. Org. Chem.* **2002**, *67*, 3142–3144; e) T. D. Avery, G. Fallon, B. W. Greatrex, S. M. Pyke, D. K. Taylor, E. R. T. Tiekink, *J. Org. Chem.* **2001**, *66*, 7955–7966; f) J. Yoshida, S. Nakatani, K. Sakaguchi, S. Isoe, *J. Org. Chem.* **1989**, *54*, 3383–3389.
[15] CCDC-276598 (for **2g**), -276597 (for **1d**), -276595 (for **1e**), and -276596 (for **1f**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[16] G. Bar, A. F. Parsons, C. B. Thomas, *Synlett* **2002**, 1069–1072.
[17] M. T. M. Clements, T. B. H. McMurry, *Can. J. Chem.* **1987**, *65*, 1810–1813.
[18] Y. Liu, Y. Zhang, *Tetrahedron* **2003**, *59*, 8429–8437.
[19] P.-K. Chiu, M. P. Sammes, *Tetrahedron* **1988**, *44*, 3531–3538.
[20] J. P. Sestelo, M. del Mar Real, L. A. Sarandeses, *J. Org. Chem.* **2001**, *66*, 1395–1402.
[21] K. Nakamura, T. Miyai, A. Nagar, S. Oka, A. Ohno, *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1179–1187.
[22] H. G. O. Becker, K. Schwetlick, Autorenkollektiv, *Organikum*, 20th ed., Wiley-VCH, Weinheim, **1999**, pp. 593.

Received: July 1, 2005
Published Online: October 19, 2005

