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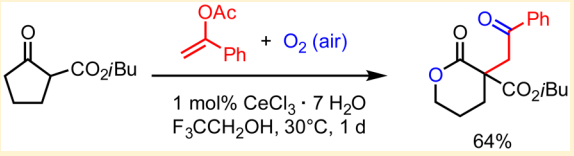
Formation of δ-Lactones by Cerium-Catalyzed, Baeyer–Villiger-Type Coupling of β-Oxoesters, Enol Acetates, and Dioxygen

Irina Geibel, Anna Dierks, Marc Schmidtmann, and Jens Christoffers*

Institut für Chemie, Carl von Ossietzky Universität Oldenburg, 26111 Oldenburg, Germany

Supporting Information

ABSTRACT: Formation of δ-lactones is observed when cyclopentanone-2-carboxylates are converted in a cerium-catalyzed reaction with α-aryl vinyl acetates under oxidative conditions. The products of this transformation possess a 1,4-dicarbonyl constitution together with a quaternary carbon center. Atmospheric oxygen is the oxidant in this process, which can be regarded as ideal from economic and ecological points of view. Further advantages of this new C–C coupling and oxidation reaction are its operational simplicity and the application of nontoxic and inexpensive $CeCl_3 \cdot 7\ H_2O$ as precatalyst. This so far unprecedented reaction is proposed to proceed via 1,2-dioxane derivatives, which decompose under formation of an oxycarbenium cation in a Baeyer–Villiger-type pathway. This mechanistic picture is supported by the observation that electron-rich (donor substituted or heteroaromatic) enol esters give higher yields than electron deficient congeners. Apart from 1,4-diketones and α-hydroxylated β-oxoesters formed as byproducts, the yields of δ-lactones range from moderate to good (up to 74%).



INTRODUCTION

The δ-lactone unit is a widely spread structural motif in natural products and pharmaceutically active compounds. Four prominent examples are warfarin (**1**),[1] an anticoagulant; the topoisomerase I inhibitor irinotecan (**2**),[2] a camptothecin derivative;[3] the antimalarial artemisinin (**3**);[4] and ochratoxin A (**4**),[5] a toxin from Aspergillus species (Figure 1). There are several strategies in the literature to prepare lactones[6] with an α-quaternary carbon center.[7] However, the most powerful method to access δ-lactone derivatives is the Baeyer–Villiger oxidation of a cyclopentanone derivative,[8] which is classically achieved by peroxycarboxylic acids,[9] although several enzymatic methods were also reported in recent years.[10]

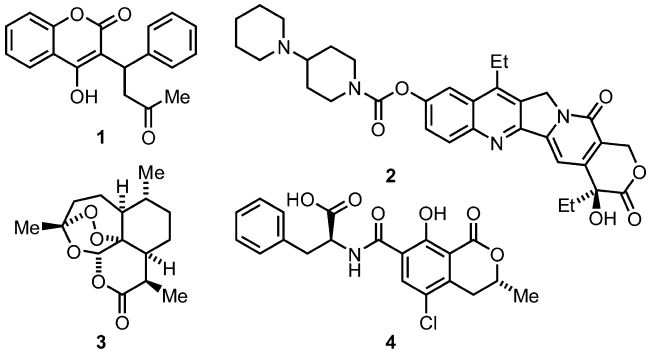
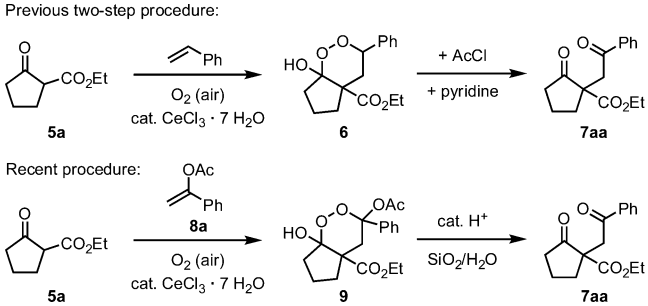


Figure 1. Examples for biologically active δ-lactone derivatives.

A couple of years ago we have reported on the preparation of 1,4-diketones **7** from β-oxoesters **5**, styrene, and molecular oxygen via 1,2-dioxane derivatives **6** (Scheme 1, top).[11] While the use of nontoxic and inexpensive $CeCl_3 \cdot 7\ H_2O$ as precatalyst and air as oxidant could classify the first step of this sequence as a contribution to the field of sustainable chemistry, this view is spoiled by the necessity of using stoichiometric amounts of pyridine and acetyl chloride in the second step, which is required for the fragmentation of the endoperoxide **6** to the final product **7**. We have recently introduced a preparative simplification by the use of enol acetates instead of styrene (Scheme 1, bottom).[12] With two acetal functions in the intermediate peroxide **9**, this material is simply hydrolyzed while acidic workup and purification. During our optimization of the latter process we have actually observed the formation of a small amount of a byproduct with *m*/*z* 290 (by GCMS), which actually differs from product **7aa** (*m*/*z* 274) by the

Scheme 1. Cerium-Catalyzed Oxidative Procedures for the Preparation of 1,4-Diketones 7 from β-Oxoesters 5[a]



[a]The older protocol required stoichiometric amounts of AcCl and pyridine for the fragmentation of the endoperoxide **6** (top). In the newer variant the two acetal functions within the intermediate product **9** are cleaved during the aqueous-acidic workup (bottom).

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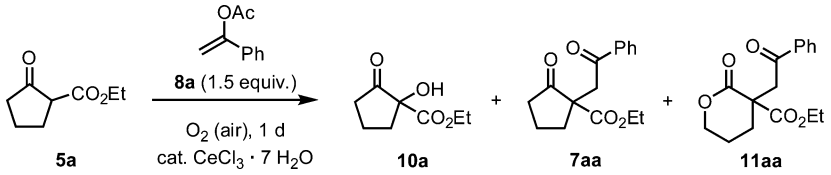
Scheme 2. Isolated Products from the Cerium-Catalyzed Conversion of Oxoester 5a with Enol Acetate 8a[a]



[a]For conditions and yields see Table 1.

incorporation of one oxygen atom. We wish to report herein on the isolation of this compound, its structure elucidation and the optimization of the reaction procedure in order to turn this oxidized compound to the major product of the transformation.

RESULTS AND DISCUSSION

An initial attempt of oxidative coupling of enol ester **8a** with oxoester **5a** (Scheme 2 and Table 1, entry 1) furnished the α-hydroxylated compound **10a** (43% yield of isolated material) as the major product[13] and the C−C coupling product **7aa** as the main byproduct (39% isolated). Another unexpected byproduct could be identified as compound **11aa** (11% after chromatography); with *m/z* 290 (GCMS) it is formally the oxidation product of compound **7aa** (*m/z* 274). After elucidation of the δ-lactone constitution (*vide infra*) we considered it to be a valuable target for optimization of reaction parameters. In the following screening program we investigated the influence of the reaction temperature (varied in the range of 20 to 70 °C) and the relative amount of precatalyst $CeCl_3 \cdot 7\ H_2O$ (10, 5, 2.5, 1, 0.5, 0.3, and 0 mol%, respectively) on the yield of compound **11aa**. The choice of the solvent turned out to be essential, as was already investigated in the preceding work on formation of 1,4-diketones 7.[12] Only the solvents showing significant conversions toward 1,4-diketones 7 also gave the derived lactones **11**, as were the following: *i*PrOH, hexafluoroisopropanol (HFIP) and 2,2,2-trifluoroethanol (TFE). Interestingly, the beneficial effects of fluorinated solvents in catalysis as well as in oxidation reactions with peroxidic intermediates are well-known.[14] In general, the screening was performed on a GC-scale, but in selected cases products were isolated by column chromatography to obtain a value for the yield of isolated material (see footnotes a and b of Table 1). Some representative results of the optimization program are listed in Table 1: First of all, with a small increase of the reaction temperature, the 1,4-diketone **7aa** became the major product of the conversion (entry 2, 61% by GC). The change of solvent to HFIP turned the selectivity toward the lactone **11aa** (entry 4, 42% isolated). Finally, the optimal results for the formation of compound **11aa** (59% isolated) were obtained by lowering the amount of precatalyst (1 mol%, entry 8). In this case no α-hydroxylated product **10a** was formed and the 1,4-diketone **7aa** was the only byproduct (21% yield after chromatography). Further lowering of the amount of precatalyst did not improve the yield of the target compound **11aa** (entry 9). Without cerium salt in the reaction mixture, no conversion was observed (entry 10). The crucial role of the Ce(III)/Ce(IV) redox system for the α-oxidation of β-oxoesters[15] as well as the formation of the 1,2-dioxane derivatives was discussed by us before.[11d] It is however clear, that Ce^{3+} could also act as a Lewis acid under reaction conditions.[16] Some nickel, cobalt, copper and manganese salts, which are known to catalyze the α-hydroxylation reaction of β-oxoesters,[17] have also been investigated as precatalysts. The respective results were always significantly inferior to those obtained with cerium chloride (see Supporting Information for details).

Table 1. Optimization of the Reaction Parameters (Representative Examples)

entry	$CeCl_3 \cdot 7\ H_2O$	solvent	*T*	yield (**10a**)	yield (**7aa**)	yield (**11aa**)
1	5 mol%	*i*PrOH	23 °C	43%[a]	39%[a]	11%[a]
2	5 mol%	*i*PrOH	30 °C	[b]	61%[b]	7%[b]
3	5 mol%	HFIP	30 °C	[b]	19%[b]	41%[b]
4	5 mol%	HFIP	30 °C	22%[a]	12%[a]	42%[a]
5	5 mol%	TFE	30 °C	[b]	49%[b]	36%[b]
6	5 mol%	TFE	50 °C	[b]	52%[b]	30%[b]
7	1 mol%	TFE	30 °C	[b]	29%[b]	59%[b]
8	1 mol%	TFE	30 °C	0%[a]	21%[a]	59%[a]
9	0.5 mol%	TFE	30 °C	[b]	15%[b]	46%[b]
10	0 mol%	TFE	30 °C	[b]	0%[b]	0%[b]

[a]Yields of isolated products after chromatographic purification. [b]Yields determined by GC with mesitylene as internal standard; the amount of α-hydroxylated compound **10a** could not be determined with certainty because of lacking baseline resolution with enol ester **8a**.

The constitution of lactone **11aa** was already indicated by ^{1}H NMR spectroscopy by the characteristic signals of the two diastereotopic OCH_2 protons (δ = 4.56 and 4.70 ppm). In order to obtain crystalline materials, the *para*-bromo substituted enol acetate **8b** (for its preparation see below) was converted with oxoester **5a** to give the products **7ab** and **11ab** both as solid materials, which contained suitable single crystals for X-ray analysis;[18] ORTEP-representations of their structures in the solid state are given in Figures 2 and 3. As indicated initially by the difference in molar mass (Δ*m/z* 16), both compounds only differ in the replacement of the cyclopentanone ring by a δ-lactone unit.

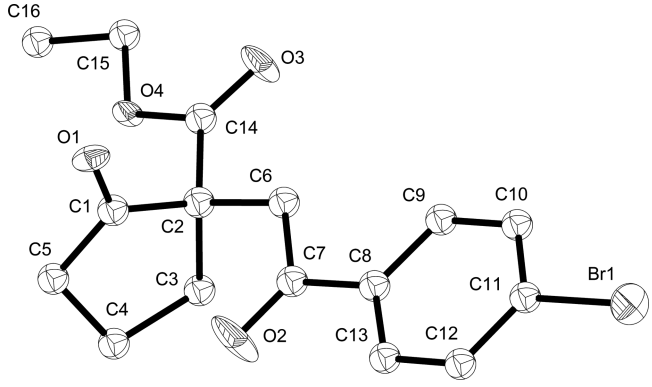


Figure 2. ORTEP-representation of the molecular structure of 1,4-diketone **7ab** in the solid state, ellipsoids of hetero atoms at the 50% probability level, H atoms omitted for clarity.

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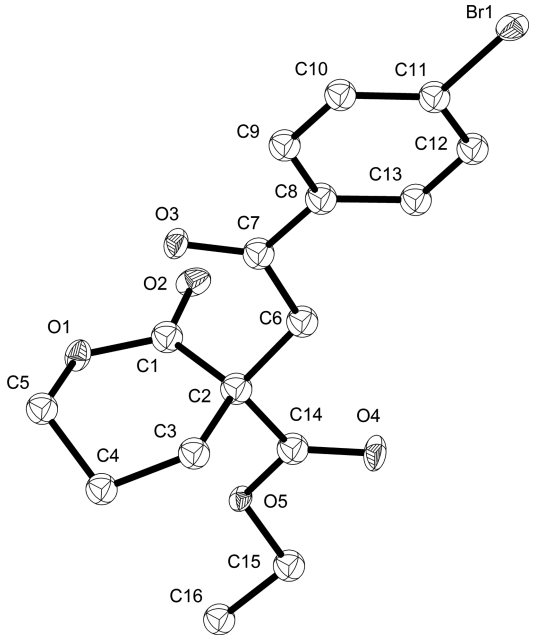
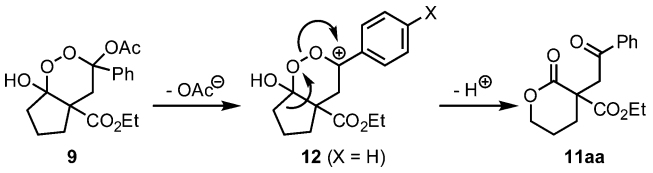


Figure 3. ORTEP-representation of the molecular structure of δ-lactone **11ab** in the solid state, ellipsoids of hetero atoms at the 50% probability level, H atoms omitted for clarity.

As a mechanistic rationale for the formation of a δ-lactone from endoperoxidic intermediate **9** we propose the loss of an acetate ion under formation of an oxycarbenium ion **12**. One might speculate, whether this elimination could either be facilitated by the relatively high acidity of the solvent[14] or even with the aid of Ce^{3+} as a Lewis acid.[16] Anyhow, cationic species **12** could actually decompose in analogy to a Baeyer–Villiger reaction pathway with migration of the primary carbon atom under ring expansion. The migrating carbon atom is in antiperiplanar conformation to the leaving oxygen atom within the 1,2-dioxane ring, which is a perfect prerequisite for this rearrangement reaction. An alternative pathway might actually be the migration of the quaternary carbon center, which would be slightly disfavored due to the electron withdrawing effect of the ester moiety. A similar regioselectivity was at least once reported before for an α-methoxycarbonyl-α-methylcyclopentanone derivative.[19] In order to support this mechanistic picture we suggested introducing electron donating or withdrawing groups X at the *para*-position of the phenyl ring in order to either stabilize or destabilize the benzylic cation **12**. The results (see Scheme 4 and Table 2) clearly indicated that a cationic intermediate, such as compound **12**, is highly probable. Furthermore, if isopropenyl acetate is used as enol ester, no formation of lactone byproduct is observed, which is another indication for the requirement of benzylic stabilization of a cationic intermediate **12**.

The scope of the lactone formation was investigated by variation of the ring size and the alkyl groups of the β-oxoesters **5x**. Furthermore, we have broadly varied the aromatic residue Ar of the enol acetate **8y** in order to support the mechanistic picture drawn in Scheme 3. All reactions were performed under the optimized conditions (Scheme 4). First of all, the aromatic residues of the enol acetates **8y** were varied in order to get insight into the mechanistic proposal given in Scheme 3. Entry 1 of Table 2 is the repetition of the result from Table 1. The reaction of *para*-bromo derivative **8b** was performed in order to get crystalline products **11ab** (44%) and **7ab** (19%, entry 2)

Scheme 3. Mechanistic Proposal for the Formation of δ-Lactone 11aa from Endoperoxide 9 via Oxycarbenium Ion 12



9 **12** (X = H) **11aa**

suitable for single X-ray crystal structure analysis (see above); a relatively large amount of the α-hydroxylated compound **10a** (35%) was formed in this case. The results of the next four experiments supported the mechanistic picture drawn in Scheme 3: Introduction of the electron donating *para*-methoxy substituent enlarged the yield of the lactone **11ac** (66%, entry 3), whereas it got lower when electron withdrawing fluorine substituents are introduced (**11ad**, 47% and **11ae**, 38%; entries 4 and 5). With a *para*-nitro substitution the yields completely collapsed (**11af**, 7%; entry 6). The reaction also tolerated electron-rich, heteroaromatic residues within the enol esters, as results in entries 7–9 show: With thiophene and furane derivatives **8g** and **8h**, the yield of lactones is reasonable (55% in both cases). Interestingly, no α-hydroxylated product **10a** was formed in these cases. With an *N*-tosyl pyrrole moiety, the yield decreased (product **11ai**, 36%, entry 9). We then took a brief look to other alkyl residues at the oxoester and found that the isobutyl ester **5b** gave an improvement of yields (products **11ba**, 64% and **11bc**, 74%; entries 10 and 11). With other ring sizes at the oxoester starting material (six and seven membered ring **5c** and **5d**, respectively), the conversion gave almost no lactone product; the 1,4-diketones **7ca** (41%) and **7da** (45%, entries 12 and 13) are the major products in these cases. Conversion of a α-acetylcyclopentanone (**5e**) as a β-diketone gave no lactone **11ea** under standard conditions. It was however obtained in insignificant amounts (14% together with 24% 1,4-diketone **7ea**) when the reaction temperature and time were enhanced (entry 14).

Enol acetates were prepared following two literature protocols as is exemplified with procedures for the two new compounds **8e** and **8i** in the Experimental Section: The respective acetophenone derivative was deprotonated with LiHMDS at −78 °C in THF solution and the respective lithium enolate trapped with AcCl at the same temperature.[20] This method was applied for the preparation of compounds **8d** and **8e**. Alternatively, the acetophenone derivative was equilibrated with catalytic amounts of either H_2SO_4 or *p*TosOH in an excess of isopropenylacetate as acetyl donor and the mixture separated by fractional distillation or column chromatography.[21] This protocol was actually preferred due to its operational simplicity and applied for the preparation of compounds **8a**, **8b**, **8c**, **8f** (with H_2SO_4), and **8g**, **8h**, **8i** (with *p*TosOH).

CONCLUSION

We have introduced a so far unprecedented transformation of cyclopentanone-2-carboxylates **5a** and **5b** with α-aryl vinyl acetates **8a–8f** furnishing eleven new δ-lactones **11** as products, which hold a 1,4-dicarbonyl constitution and have a quaternary carbon center in their 2-position. As byproducts, 1,4-diketones **7** and α-hydroxylated products **10a** and **10b** were formed, which could be separated by column chromatography. The yields of lactones ranged from 74% with a donor substituted

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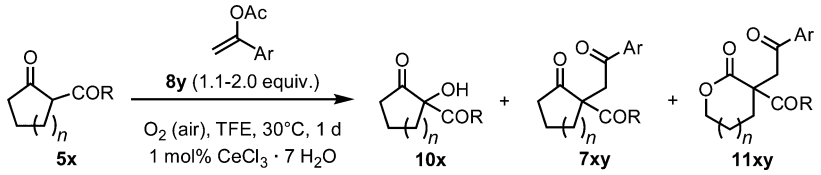
Scheme 4. Conversion of β-Oxoesters 5x with Enolacetates 8y Giving α-Hydroxy Compounds 10x, 1,4-Diketones 7xy, or Lactones 11xy[a]



[a]For **x**, **y**, *n*, R, Ar, and yields see Table 2.

Table 2. Results for Different Oxoesters 5x and Enol Acetates 8y

entry	5x (*n*, R)	8y (Ar)	yields[a]		
1	**5a** (1, OEt)	**8a** (Ph)	59% (**11aa**),	21% (**7aa**),	0% (**10a**)
2	**5a** (1, OEt)	**8b** (4-BrC_6H_4)	44% (**11ab**),	19% (**7ab**),	35% (**10a**)
3	**5a** (1, OEt)	**8c** (4-MeOC_6H_4)	66% (**11ac**),	15% (**7ac**),	7% (**10a**)
4	**5a** (1, OEt)	**8d** [3,5-$(CF_3)_2C_6H_3$]	47% (**11ad**),	21% (**7ad**),	19% (**10a**)
5	**5a** (1, OEt)	**8e** (2,4-$F_2C_6H_3$)	38% (**11ae**),	22% (**7ae**),	32% (**10a**)
6	**5a** (1, OEt)	**8f** (4-$NO_2C_6H_4$)	7% (**11af**),	2% (**7af**),	36% (**10a**)
7	**5a** (1, OEt)	**8g** (2-thienyl)	55% (**11ag**),	18% (**7ag**),	0% (**10a**)
8	**5a** (1, OEt)	**8h** (2-furyl)	55% (**11ah**),	20% (**7ah**),	0% (**10a**)
9	**5a** (1, OEt)	**8i** (*N*-Tos-2-pyrrolyl)	36% (**11ai**),	16% (**7ai**),	24% (**10a**)
10	**5b** (1, O*i*Bu)	**8a** (Ph)	64% (**11ba**),	29% (**7ba**),	7% (**10b**)
11	**5b** (1, O*i*Bu)	**8c** (4-MeOC_6H_4)	74% (**11bc**),	21% (**7bc**),	2% (**10b**)
12	**5c** (2, OEt)	**8a** (Ph)	9% (**11ca**),	41% (**7ca**),	9% (**10c**)
13	**5d** (3, OMe)	**8a** (Ph)	0% (**11da**),	45% (**7da**),	4% (**10d**)
14[b]	**5e** (1, Me)	**8a** (Ph)	14% (**11ea**),	24% (**7ea**),	0% (**10e**)

[a]Yields of isolated products after chromatographic purification. [b]Different reaction conditions: 1 mol% $CeCl_3 \cdot 7\ H_2O$, TFE, 50 °C, 3 d.

aromatic residue (4-MeOC_6H_4) at enol ester **8c** (product **11bc**) to 38% with an electron deficient enol ester **8e** (difluorophenyl-substitution, product **11ae**); with a nitrophenyl-ring, the yields broke down (7% of product **11af**). With this reactivity profile, the mechanistic picture, which proposes the decomposition of an intermediate 1,2-dioxane derivative **9** under formation of an aryl-substituted oxycarbenium ion **12**, was supported. Among the enol acetates used, also three heteroaromatic examples were investigated, which gave 55% (thiophene and furane derivatives) and 36% (*N*-tosylpyrrole) yield of lactones. Despite the frugality of the starting materials, the constitution of the products is highly interesting. Further advantages of this new C−C coupling and oxidation reaction are its operational simplicity and the application of nontoxic and inexpensive $CeCl_3 \cdot 7\ H_2O$ as precatalyst and atmospheric oxygen as the oxidant, which can be regarded as ideal from economic and ecological points of view.

EXPERIMENTAL SECTION

General. Preparative column chromatography was carried out using Merck SiO_2 (35−70 μm, type 60 A) with hexanes, *tert*-butyl methyl ether (MTBE), and ethyl acetate (EtOAc) as eluents. TLC was performed on aluminum plates coated with SiO_2 F_{254}. ^{1}H-, ^{19}F-, and ^{13}C NMR spectra were recorded on 500 and 300 MHz instruments. Multiplicities of carbon signals were determined with DEPT experiments. HRMS spectra were obtained with an ESI spectrometer (pos. mode) with Q-TOF analyzer. IR spectra were recorded on a spectrometer equipped with a diamond ATR unit. The starting materials **5a**, **5c**, **5d**, **5e**, and 2,4-difluoroacetophenone were commercially available. The following compounds were literature known and prepared according to published procedures: **5b**,[22] **8a**,[12] **8b**,[21,23] **8c**,[12] **8d**,[20,24] **8f**,[12] **8g**,[25] **8h**,[26] and 2-acetyl-*N*-tosylpyrrole.[27]

1-(2,4-Difluorophenyl)vinyl Acetate (8e). The procedure was performed according to a literature procedure.[20] Under exclusion of air and moisture (nitrogen atmosphere) and at −78 °C, a solution of 2,4-difluoroacetophenone (2.00 g, 12.8 mmol) in abs. THF (10 mL) was dropwise added within 30 min to a solution of LiHMDS (14.1 mL of a 1.0 mol/L solution THF, 14.1 mmol; diluted with 40 mL abs. THF). After stirring the mixture for another 15 min at −78 °C, a solution of AcCl (1.11 g, 14.1 mmol) in abs. THF (10 mL) was added and the resulting mixture allowed for warming to ambient temperature within 1 h. Ethyl acetate (50 mL) was added and the mixture filtered through (SiO_2, washing with 50 mL EtOAc). The filtrate was evaporated and the residue chromatographed (SiO_2, hexanes/MTBE 3:1, R_f = 0.54) to furnish enolester **8e** (729 mg, 3.68 mmol, 29%) as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.23 (s, 3H), 5.20−5.21 (m, 1H), 5.47−5.48 (m, 1H), 6.81−6.88 (m, 2H), 7.35 (td, J = 8.8 Hz, J = 6.4 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 20.8 (CH_3), 104.7 (t, $^2J_{C,F}$ = 26.1 Hz, CH), 107.3 (d, $^4J_{C,F}$ = 8.2 Hz, CH_2), 111.4 (dd, $^2J_{C,F}$ = 21.5 Hz, $^4J_{C,F}$ = 3.8 Hz, CH), 119.1 (dd, $^2J_{C,F}$ = 11.7 Hz, $^4J_{C,F}$ = 4.1 Hz, C), 129.2 (dd, $^3J_{C,F}$ = 9.8 Hz, $^3J_{C,F}$ = 4.1 Hz, CH), 147.1 (d, $^3J_{C,F}$ = 3.3 Hz, C), 160.1 (dd, $^1J_{C,F}$ = 254.2 Hz, $^3J_{C,F}$ = 11.3 Hz, CF), 162.8 (dd, $^1J_{C,F}$ = 252.1 Hz, $^3J_{C,F}$ = 12.7 Hz, CF), 168.8 (C) ppm. ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$): δ = −108.8 (d, J = 9.2 Hz, 1F), −109.0 (d, J = 9.2 Hz, 1F) ppm. IR (ATR): λ^{-1} = 2938 (w), 1740 (m), 1676 (m), 1610 (vs), 1498 (s), 1423 (s), 1370 (m), 1268 (s), 1234 (s), 1201 (m), 1141 (s), 1099 (s), 1076 (m), 1013 (m), 968 (vs), 848 (vs), 816 (s), 734 (m), 613 (s) cm^{-1}. HRMS (ESI): calcd. 221.0385 (for $C_{10}H_8F_2NaO_2^+$); found 221.0389 [M+Na$^+$]. $C_{10}H_8F_2O_2$ (198.17).

2-(1-Acetoxyvinyl)-1-(4-methylphenylsulfonyl)pyrrole (8i). The procedure was performed according to a literature procedure.[25] A mixture of 2-acetyl-1-tosylpyrrole (1.00 g, 3.80 mmol), isopropenyl acetate (1.90 g, 19.0 mmol), and *p*TosOH·H_2O (51 mg, 0.27 mmol) was stirred for 16 h at 100 °C. Subsequently, all volatiles were removed in vacuum and the residue was chromatographed (SiO_2, hexanes/MTBE 3:2, R_f = 0.32) to yield the enol ester **8i** (600 mg, 1.96 mmol, 52%) as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.02 (s, 3H), 2.39 (s, 3H), 5.08 (d, J = 1.5 Hz, 1H), 5.20 (d, J = 1.5 Hz, 1H), 6.22 (t, J = 3.4 Hz, 1H), 6.40 (dd, J = 3.4 Hz, J = 1.8 Hz, 1H), 7.26−7.27 (m,

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2H), 7.32 (dd, J = 3.4 Hz, J = 1.8 Hz, 1H), 7.68−7.71 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 21.1 (CH_3), 21.6 (CH_3), 108.8 (CH_2), 111.9 (CH), 118.6 (CH), 124.9 (CH), 127.2 (2 CH), 129.5 (C), 129.6 (2 CH), 135.8 (C), 144.2 (C), 145.0 (C), 168.6 (C) ppm. IR (ATR): λ^{-1} = 3149 (w), 3135 (w), 2930 (w), 1758 (m), 1710 (w), 1679 (w), 1596 (w), 1437 (w), 1365 (s), 1204 (m), 1172 (vs), 1144 (vs), 1084 (s), 1048 (m), 1018 (m), 956 (w), 935 (w), 889 (w), 813 (m), 734 (m), 703 (w), 671 (vs) cm^{-1}. HRMS (ESI): calcd. 328.0614 (for $C_{15}H_{15}NNaO_4S^+$); found 328.0627 [M+Na^+]. $C_{15}H_{15}NO_4S$ (305.35).

Ethyl 3-(2-Oxo-2-phenylethyl)tetrahydropyran-2-one-3-carboxylate (11aa). $CeCl_3{\cdot}7\ H_2O$ (6 mg, 15 μmol) was added to a mixture of β-oxoester **5a** (240 mg, 1.54 mmol) and enol ester **8a** (378 mg, 2.33 mmol, 1.5 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 3:1 → 1:1) to yield 1,4-diketone **7aa** [89 mg, 0.32 mmol, 21%, R_f = 0.40 (hexanes/MTBE 1:1)] as a colorless oil. Second, the title compound **11aa** [261 mg, 0.90 mmol, 59%, R_f = 0.19 (hexanes/MTBE = 1:1)] was eluted as a colorless oil.

Lactone 11aa. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.1 Hz, 3H), 1.84−1.89 (m, 1H), 2.09−2.25 (m, 3H), 3.62 (d, J = 18.6 Hz, 1H), 4.03 (d, J = 18.6 Hz, 1H), 4.19−4.31 (m, 2H), 4.54−4.57 (m, 1H), 4.67−4.73 (m, 1H), 7.44−7.47 (m, 2H), 7.55−7.58 (m, 1H), 7.95−7.96 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.0 (CH_2), 30.3 (CH_2), 45.7 (CH_2), 51.0 (C), 62.3 (CH_2), 70.0 (CH_2), 128.0 (2 CH), 128.6 (2 CH) 133.6 (CH), 136.0 (C), 169.8 (C), 171.4 (C), 196.7 (C) ppm. IR (ATR): λ^{-1} = 2978 (w), 2934 (w), 1718 (vs), 1689 (vs), 1597 (w), 1580 (w), 1449 (m), 1405 (m), 1353 (m), 1297 (m), 1282 (m), 1251 (m), 1197 (s), 1166 (m), 1138 (w), 1117 (m), 1099 (m), 1068 (m), 1022 (m), 1002 (m), 985 (s), 939 (w), 857 (m), 753 (s), 690 (s), 639 (m), 584 (m) cm^{-1}. HRMS (ESI): calcd. 313.1047 (for $C_{16}H_{18}NaO_5^+$); found 313.1046 [M+Na^+]. $C_{16}H_{18}O_5$ (290.32)

Ethyl 2-(2-Oxo-2-phenylethyl)cyclopentanone-2-carboxylate (7aa). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.22 (t, J = 7.1 Hz, 3H), 2.04−2.20 (m, 3H), 2.47−2.53 (m, 1H), 2.57−2.67 (m, 2H), 3.46 (d, J = 18.5 Hz, 1H), 3.84 (d, J = 18.5 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 7.42−7.45 (m, 2H), 7.54−7.57 (m, 1H), 7.92−7.94 (m, 2H) ppm. The data were in accordance with literature values.[12]

Ethyl 3-[2-Oxo-2-(4-bromophenyl)ethyl]tetrahydropyran-2-one-3-carboxylate (11ab). $CeCl_3{\cdot}7\ H_2O$ (3 mg, 8 μmol) was added to a mixture of β-oxoester **5a** (127 mg, 0.82 mmol) and enol ester **8b** (298 mg, 1.23 mmol, 1.5 equiv) in TFE (0.5 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 3:1 → 1:1) to yield 1,4-diketone **7ab** [54 mg, 0.15 mmol, 19%, R_f = 0.44 (hexanes/MTBE 1:1)] as a yellow solid (mp 103 °C). Second, the α-hydroxylated compound **10a** [49 mmol, 0.28 mmol, 35%, R_f = 0.33 (hexanes/MTBE 1:1)]) was obtained as a colorless oil. As a third fraction the title compound **11ab** [134 mg, 0.36 mmol, 44%, R_f = 0.18 (hexanes/MTBE 1:1)] was eluted as a colorless solid (mp 78 °C).

Lactone 11ab. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.31 (t, J = 7.1 Hz, 3H), 1.84−1.90 (m, 1H), 2.10−2.27 (m, 3H), 3.56 (d, J = 18.6 Hz, 1H), 4.00 (d, J = 18.5 Hz, 1H), 4.20−4.32 (m, 2H), 4.55−4.58 (m, 1H), 4.66−4.71 (m, 1H), 7.59−7.62 (m, 2H), 7.81−7.84 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.1 (CH_2), 30.3 (CH_2), 45.7 (CH_2), 51.1 (C), 62.4 (CH_2), 70.0 (CH_2), 128.9 (C), 129.6 (2 CH), 132.0 (2 CH), 134.8 (C), 169.8 (C), 171.4 (C), 195.8 (C) ppm. IR (ATR): λ^{-1} = 3004 (m), 2979 (m), 2938 (m), 2870 (w), 1726 (s), 1712 (vs), 1686 (s), 1583 (s), 1567 (m), 1470 (m), 1455 (m), 1441 (m), 1396 (s), 1346 (m), 1281 (m), 1247 (s), 1210 (w), 1194 (s), 1166 (s), 1141 (m), 1098 (m), 1068 (s), 1020 (m), 999 (s), 985 (m), 968 (m), 903 (m), 858 (s), 838 (m), 813 (s), 761 (w), 716 (m), 637 (s) cm^{-1}. HRMS (ESI): calcd. 391.0152 (for $C_{16}H_{17}{}^{79}BrNaO_5^+$); found 391.0146 [M+$Na^+$]. $C_{16}H_{17}BrO_5$ (369.21).

Ethyl 2-[2-Oxo-2-(4-bromophenyl)ethyl]cyclopentanone-2-carboxylate (7ab). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.1 Hz, 3H), 2.04−2.22 (m, 3H), 2.49−2.67 (m, 3H), 3.41 (d, J = 18.5 Hz, 1H), 3.79 (d, J = 18.6 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 7.58−7.61 (m, 2H), 7.78−7.81 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.8 (CH_2), 33.4 (CH_2), 37.7 (CH_2), 43.3 (CH_2), 57.4 (C), 61.7 (CH_2), 128.7 (C), 129.5 (2 CH), 131.9 (2 CH), 135.0 (C), 170.6 (C), 195.8 (C), 214.9 (C) ppm. IR (ATR): λ^{-1} = 2983 (m), 2960 (m), 2928 (m), 1762 (m), 1740 (vs), 1720 (vs), 1688 (vs), 1651 (m), 1583 (s), 1568 (m), 1486 (m), 1467 (m), 1443 (m), 1396 (s), 1368 (m), 1327 (m), 1259 (m), 1202 (s), 1155 (vs), 1091 (m), 1066 (m), 1044 (m), 1007 (s), 990 (s), 962 (m), 862 (m), 844 (m), 815 (s), 712 (w) cm^{-1}. HRMS (ESI): calcd. 375.0208 (for $C_{16}H_{17}{}^{79}BrNaO_4^+$); found 375.0216 [M+$Na^+$]. $C_{16}H_{17}BrO_4$ (353.21).

Ethyl 2-Hydroxycyclopentanone-2-carboxylate (10a). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.1 Hz, 3H), 2.08−2.14 (m, 3H), 2.43−2.53 (m, 3H), 3.63 (s, 1H), 4.23−4.28 (m, 2H) ppm. The data were in accordance with literature values.[13b]

Ethyl 3-[2-Oxo-2-(4-methoxyphenyl)ethyl]tetrahydropyran-2-one-3-carboxylate (11ac). $CeCl_3{\cdot}7\ H_2O$ (6 mg, 15 μmol) was added to a mixture of β-oxoester **5a** (237 mg, 1.51 mmol) and enol ester **8c** (444 mg, 2.31 mmol, 1.5 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 2:1 → 1:1) to yield 1,4-diketone **7ac** [67 mg, 0.22 mmol, 15%, R_f = 0.34 (hexanes/MTBE 1:1)] as a colorless oil. Second, the α-hydroxylated compound **10a** [18 mg, 0.10 mmol, 7%, R_f = 0.31 (hexanes/MTBE 1:1)]) was obtained as a colorless oil. As a third fraction the title compound **11ac** [320 mg, 0.99 mmol, 66%, R_f = 0.10 (hexanes/MTBE 1:1)] was eluted as a colorless oil.

Lactone 11ac. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.1 Hz, 3H), 1.83−1.88 (m, 1H), 2.09−2.24 (m, 3H), 3.57 (d, J = 18.4 Hz, 1H), 3.86 (s, 3H), 3.99 (d, J = 18.3 Hz, 1H), 4.19−4.31 (m, 2H), 4.52−4.56 (m, 1H), 4.67−4.72 (m, 1H), 6.90−6.93 (m, 2H), 7.92−7.95 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.1 (CH_2), 30.3 (CH_2), 45.4 (CH_2), 51.1 (C), 55.4 (CH_3), 62.2 (CH_2), 69.9 (CH_2), 113.7 (2 CH), 129.3 (C), 130.3 (2 CH), 163.8 (C), 169.8 (C), 171.6 (C), 195.1 (C) ppm. IR (ATR): λ^{-1} = 2958 (w), 2924 (m), 2853 (w), 1721 (vs), 1673 (s), 1600 (vs), 1575 (w), 1511 (w), 1457 (m), 1421 (w), 1407 (w), 1353 (m), 1282 (w), 1251 (s), 1198 (m), 1167 (vs), 1115 (m), 1026 (m), 997 (m), 987 (m), 831 (m), 640 (w) cm^{-1}. HRMS (ESI): calcd. 343.1152 (for $C_{17}H_{20}NaO_6^+$); found 343.1159 [M+Na^+]. $C_{17}H_{20}O_6$ (320.35).

Ethyl 2-[2-Oxo-2-(4-methoxyphenyl)ethyl]cyclopentanone-2-carboxylate (7ac). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.22 (t, J = 7.1 Hz, 3H), 2.04−2.19 (m, 3H), 2.42−2.53 (m, 1H), 2.57−2.65 (m, 2H), 3.43 (d, J = 18.3 Hz, 1H), 3.78 (d, J = 18.3 Hz, 1H), 3.85 (s, 3H), 4.15 (q, J = 7.1 Hz, 2H), 6.89−6.92 (m, 2H), 7.89−7.92 (m, 2H) ppm. The data were in accordance with literature values.[12]

Ethyl 3-{2-Oxo-2-[3,5-bis(trifluoromethyl)phenyl]ethyl}-tetrahydropyran-2-one-3-carboxylate (11ad). $CeCl_3{\cdot}7\ H_2O$ (2 mg, 5 μmol) was added to a mixture of β-oxoester **5a** (82 mg, 0.53 mmol) and enol ester **8d** (204 mg, 0.68 mmol, 1.3 equiv) in TFE (0.4 mL), and the reaction mixture was stirred at 30 °C for 22 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 1:1) to yield 1,4-diketone **7ad** (45 mg, 0.11 mmol, 21%, R_f = 0.55) as a colorless oil. Second, the α-hydroxylated compound **10a** (18 mg, 0.10 mmol, 19%, R_f = 0.34) was obtained as a colorless oil. As a third fraction the title compound **11ad** (106 mg, 0.25 mmol, 47%, R_f = 0.29) was eluted as a colorless oil.

Lactone 11ad. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.1 Hz, 3H), 1.89−1.95 (m, 1H), 2.16−2.24 (m, 3H), 3.61 (d, J = 18.6 Hz, 1H), 4.04 (d, J = 18.6 Hz, 1H), 4.22−4.34 (m, 2H), 4.56−4.60 (m, 1H), 4.64−4.69 (m, 1H), 8.08 (s, 1H), 8.39 (s, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.0 (CH_2), 30.3 (CH_2), 45.7 (CH_2), 51.3 (C), 62.6 (CH_2), 70.1 (CH_2), 122.8 (q, $^1J_{CF}$ = 273.1 Hz, 2 CF_3), 126.7−126.8 (m, CH), 128.1 (q, $^3J_{CF}$ = 4.0 Hz, 2 CH), 132.5 (q, $^2J_{CF}$ = 34.1 Hz, 2 C), 137.6 (C), 169.4 (C), 171.1 (C), 194.4

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(C) ppm. $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$): δ = −63.0 (s, 2 CF_3) ppm. IR (ATR): λ^{-1} = 2981 (w), 1726 (m), 1670 (m), 1620 (w), 1453 (w), 1371 (w), 1349 (w), 1276 (s), 1250 (m), 1170 (s), 1126 (s), 1020 (w), 988 (w), 902 (m), 844 (m), 699 (m), 681 (s) cm^{-1}. HRMS (ESI): calcd. 449.0794 (for $C_{18}H_{16}F_6NaO_5^+$); found 449.0801 [M+Na^+]. $C_{18}H_{16}F_6O_5$ (426.31).

Ethyl 2-{2-Oxo-2-[3,5-bis(trifluoromethyl)phenyl]ethyl}-cyclopentanone-2-carboxylate (7ad). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.24 (t, J = 7.1 Hz, 3H), 2.07−2.15 (m, 2H), 2.18−2.26 (m, 1H), 2.55−2.58 (m, 2H), 2.67−2.72 (m, 1H), 3.43 (d, J = 18.6 Hz, 1H), 3.85 (d, J = 18.6 Hz, 1H), 4.14−4.23 (m, 2H), 8.07 (s, 1H), 8.37 (s, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.8 (CH_2), 33.4 (CH_2), 37.6 (CH_2), 43.3 (CH_2), 57.5 (C), 61.9 (CH_2), 122.8 (q, $^1J_{CF}$ = 273.2 Hz, 2 CF_3), 126.5−126.6 (m, CH), 128.1 (q, $^3J_{CF}$ = 4.1 Hz, 2 CH), 132.5 (q, $^2J_{CF}$ = 34.0 Hz, 2 C), 137.9 (C), 170.3 (C), 194.3 (C), 214.3 (C) ppm. $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$): δ = −63.1 (s, 2 CF_3) ppm. IR (ATR): λ^{-1} = 2986 (w), 1754 (m), 1726 (m), 1704 (m), 1621 (w), 1453 (w), 1388 (w), 1345 (w), 1278 (s), 1174 (s), 1230 (s), 1229 (w), 911 (m), 845 (m), 701 (m), 683 (s) cm^{-1}. HRMS (ESI): calcd. 433.0845 (for $C_{18}H_{16}F_6NaO_4^+$); found 433.0847 [M+Na^+]. $C_{18}H_{16}F_6O_4$ (410.31).

Ethyl 3-[2-Oxo-2-(2,4-difluorophenyl)ethyl]-tetrahydropyran-2-one-3-carboxylate (11ae). $CeCl_3{\cdot}7\ H_2O$ (5 mg, 13 μmol) was added to a mixture of β-oxoester **5a** (240 mg, 1.54 mmol) and enol ester **8e** (455 mg, 2.29 mmol, 1.5 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 3:1 → 1:1) to yield 1,4-diketone **7ae** [103 mg, 0.33 mmol, 22%, R_f = 0.50 (hexanes/MTBE 1:1)] as a colorless oil. Second, the α-hydroxylated compound **10a** [85 mg, 0.49 mmol, 32%, R_f = 0.32 (hexanes/MTBE 1:1)]) was obtained as a colorless oil. As a third fraction the title compound **11ae** [190 mg, 0.58 mmol, 38%, R_f = 0.25 (hexanes/MTBE 1:1)] was eluted as a colorless oil.

Lactone 11ae. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.27 (t, J = 7.1 Hz, 3H), 1.81−1.88 (m, 1H), 2.10−2.18 (m, 3H), 3.52 (dd, J = 19.2 Hz, J = 3.7 Hz, 1H), 3.95 (dd, J = 19.2 Hz, J = 3.4 Hz, 1H), 4.17−4.28 (m, 2H), 4.50−4.54 (m, 1H), 4.60−4.65 (m, 1H), 6.86 (ddd, J_{HF} = 11.1 Hz, J_{HF} = 8.6 Hz, J_{HH} = 2.4 Hz, 1H), 6.91−6.95 (m, 1H), 7.92 (td, J_{HF} = 8.6 Hz, J_{HH} = 6.5 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.0 (CH_2), 30.2 (CH_2), 49.9 (d, $^4J_{CF}$ = 9.1 Hz, CH_2), 51.2 (d, $^5J_{CF}$ = 2.0 Hz, C), 62.2 (CH_2), 69.9 (CH_2), 104.8 (dd, $^2J_{CF}$ = 27.7 Hz, $^2J_{CF}$ = 25.5 Hz, CH), 112.3 (dd, $^2J_{CF}$ = 21.4 Hz, $^4J_{CF}$ = 3.4 Hz, CH), 121.1 (dd, $^3J_{CF}$ = 12.8 Hz, $^4J_{CF}$ = 3.6 Hz, C), 132.6 (dd, $^3J_{CF}$ = 10.8 Hz, $^3J_{CF}$ = 3.9 Hz, CH), 162.9 (dd, $^1J_{CF}$ = 258.7 Hz, $^3J_{CF}$ = 12.7 Hz, CF), 166.1 (dd, $^1J_{CF}$ = 258.2 Hz, $^3J_{CF}$ = 12.4 Hz, CF), 169.7 (C), 171.1 (C), 193.2 (d, $^3J_{CF}$ = 4.6 Hz, C) ppm. $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$): δ = −100.5 (d, J = 12.7 Hz, 1F), − 102.8 (d, J = 12.7 Hz, 1F) ppm. IR (ATR): λ^{-1} = 2979 (w), 1739 (s), 1720 (s), 1683 (s), 1609 (s), 1497 (m), 1477 (w), 1428 (m), 1403 (m), 1356 (m), 1298 (m), 1286 (m), 1268 (m), 1250 (s), 1231 (s), 1195 (s), 1168 (m), 1141 (m), 1818 (m), 1068 (m), 1024 (m), 1004 (w), 986 (m), 969 (s), 940 (w), 906 (w), 854 (s), 819 (m), 734 (m), 703 (w) cm^{-1}. HRMS (ESI): calcd. 327.1039 (for $C_{16}H_{17}F_2O_5^+$); found 327.1056 [M+H^+]. $C_{16}H_{16}F_2O_5$ (326.30).

Ethyl 2-[2-Oxo-2-(2,4-difluorophenyl)ethyl]cyclopentanone-2-carboxylate (7ae). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.2 Hz, 3H), 2.02−2.11 (m, 2H), 2.12−2.21 (m, 1H), 2.47−2.60 (m, 2H), 2.64−2.69 (m, 1H), 3.41 (dd, J = 19.2 Hz, J = 3.4 Hz, 1H), 3.74 (dd, J = 19.1 Hz, J = 3.5 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 6.87 (ddd, J_{HF} = 11.1 Hz, J_{HF} = 8.6 Hz, J_{HH} = 2.4 Hz, 1H), 6.93−6.96 (m, 1H), 7.90 (td, J_{HF} = 8.7 Hz, J_{HH} = 6.6 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.8 (CH_2), 33.4 (CH_2), 37.6 (CH_2), 47.8 (d, $^4J_{CF}$ = 8.7 Hz, CH_2), 57.7 (d, $^5J_{CF}$ = 1.5 Hz, C), 61.6 (CH_2), 104.8 (dd, $^2J_{CF}$ = 27.7 Hz, $^2J_{CF}$ = 25.5 Hz, CH), 112.3 (dd, $^2J_{CF}$ = 21.5 Hz, $^4J_{CF}$ = 3.3 Hz, CH), 121.5 (dd, $^3J_{CF}$ = 13.2 Hz, $^4J_{CF}$ = 3.5 Hz, C), 132.6 (dd, $^3J_{CF}$ = 10.5 Hz, $^3J_{CF}$ = 4.1 Hz, CH), 162.8 (dd, $^1J_{CF}$ = 258.8 Hz, $^3J_{CF}$ = 12.5 Hz, CF), 166.0 (dd, $^1J_{CF}$ = 257.9 Hz, $^3J_{CF}$ = 12.2 Hz, CF), 170.4 (C), 193.3 (d, $^3J_{CF}$ = 4.7 Hz, C), 214.5 (C) ppm. $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$): δ = −101.1 (d, J = 12.4 Hz, 1F), − 103.0 (d, J = 12.5 Hz, 1F) ppm. IR (ATR): λ^{-1} = 2981 (w), 1753 (s), 1724 (s), 1688 (s), 1611 (s), 1500 (m), 1430 (m), 1404 (w), 1359 (m), 1323 (w), 1269 (s), 1235 (s), 1201 (m), 1144 (s), 1099 (s), 1047 (w), 1034 (w), 996 (m), 972 (s), 927 (w), 854 (s), 820 (m), 735 (m) cm^{-1}. HRMS (ESI): calcd. 311.1089 (for $C_{16}H_{17}F_2O_4^+$); found 311.1101 [M+H^+]. $C_{16}H_{16}F_2O_4$ (310.30).

Ethyl 3-[2-Oxo-2-(4-nitrophenyl)ethyl]tetrahydropyrane-2-one-3-carboxylate (11af). $CeCl_3 \cdot 7\ H_2O$ (2 mg, 5 μmol) was added to a mixture of β-oxoester **5a** (83 mg, 0.51 mmol) and enol ester **8f** (150 mg, 0.72 mmol, 1.4 equiv) in TFE (0.3 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 1:1) to yield the α-hydroxylated compound **10a** (31 mg, 0.18 mmol, 36%, R_f = 0.32) was obtained as a colorless oil. Second, the 1,4-diketone **7af** (4 mg, 0.01 mmol, 2%, R_f = 0.30) as a colorless oil. As a third fraction the title compound **11af** (12 mg, 0.04 mmol, 7%, R_f = 0.10) was eluted as a yellow solid (mp 116 °C).

Lactone 11af. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.1 Hz, 3H), 1.89−1.94 (m, 1H), 2.15−2.25 (m, 3H), 3.62 (d, J = 18.6 Hz, 1H), 4.06 (d, J = 18.6 Hz, 1H), 4.22−4.33 (m, 2H), 4.57−4.61 (m, 1H), 4.66−4.71 (m, 1H), 8.11−8.15 (m, 2H), 8.30−8.33 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.0 (CH_2), 30.3 (CH_2), 46.1 (CH_2), 51.2 (C), 62.6 (CH_2), 70.1 (CH_2), 123.9 (2 CH), 129.2 (2 CH), 140.4 (C), 150.6 (C), 169.6 (C), 171.1 (C), 195.4 (C) ppm. IR (ATR): λ^{-1} = 3115 (w), 3053 (w), 2963 (w), 2914 (w), 1739 (vs), 1708 (vs), 1682 (vs), 1600 (m), 1519 (vs), 1474 (w), 1405 (w), 1347 (vs), 1294 (m), 1244 (s), 1227 (vs), 1192 (vs), 1165 (vs), 1135 (m), 1113 (s), 1099 (s), 1063 (m), 1030 (m), 989 (m), 908 (w), 856 (s), 830 (m), 746 (s), 711 (w), 688 (m), 639 (m) cm^{-1}. HRMS (ESI): calcd. 358.0897 (for $C_{16}H_{17}NNaO_7^+$); found 358.0895 [M+Na^+]. $C_{16}H_{17}NO_7$ (335.31).

Ethyl 2-[2-Oxo-2-(4-nitrophenyl)ethyl]cyclopentanone-2-carboxylate (7af). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.1 Hz, 3H), 2.08−2.15 (m, 2H), 2.19−2.24 (m, 1H), 2.55−2.59 (m, 2H), 2.67−2.70 (m, 1H), 3.45 (d, J = 18.6 Hz, 1H), 3.85 (d, J = 18.6 Hz, 1H), 4.15−4.21 (m, 2H), 8.09−8.12 (m, 2H), 8.30−8.33 (m, 2H) ppm. The data were in accordance with literature values.[12]

Ethyl 3-[2-Oxo-2-(2-thienyl)ethyl]tetrahydropyran-2-one-3-carboxylate (11ag). $CeCl_3{\cdot}7\ H_2O$ (5 mg, 13 μmol) was added to a mixture of β-oxoester **5a** (200 mg, 1.28 mmol) and enol ester **8g** (280 mg, 1.66 mmol, 1.3 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 20 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 9:1 → 1:1) to yield the 1,4-diketone **7ag** [64 mg, 0.23 mmol, 18%, R_f = 0.41 (hexanes/MTBE 1:1)] as a colorless oil. Second, the title compound **11ag** [210 mg, 0.71 mmol, 55%, R_f = 0.18 (hexanes/MTBE 1:1)] was eluted as a yellow oil.

Lactone 11ag. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.1 Hz, 3H), 1.81−1.88 (m, 1H), 2.11−2.21 (m, 3H), 3.52 (d, J = 18.2 Hz, 1H), 3.95 (d, J = 18.2 Hz, 1H), 4.17−4.28 (m, 2H), 4.49−4.52 (m, 1H), 4.58−4.65 (m, 1H), 7.11 (dd, J = 4.9 Hz, J = 3.9 Hz, 1H), 7.64 (dd, J = 4.9 Hz, J = 0.9 Hz, 1H), 7.74 (dd, J = 3.8 Hz, J = 0.9 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 13.9 (CH_3), 21.0 (CH_2), 30.2 (CH_2), 45.8 (CH_2), 51.0 (C), 62.2 (CH_2), 69.9 (CH_2), 128.1 (CH), 132.4 (CH), 134.1 (CH), 143.1 (C), 169.5 (C), 171.2 (C), 189.5 (C) ppm. IR (ATR): λ^{-1} = 3093 (w), 2975 (w), 2934 (w), 1716 (vs), 1657 (s), 1519 (w), 1453 (w), 1414 (s), 1360 (m), 1281 (m), 1252 (m), 1222 (m), 1196 (s), 1166 (m), 1137 (w), 1117 (m), 1068 (w), 1058 (w), 1021 (m), 986 (m), 951 (w), 856 (m), 823 (w), 730 (s), 638 (w) cm^{-1}. HRMS (ESI): calcd. 319.0611 (for $C_{14}H_{16}NaO_5S^+$); found 319.0618 [M+Na^+]. $C_{14}H_{16}O_5S$ (296.34).

Ethyl 2-[2-Oxo-2-(2-thienyl)ethyl]cyclopentanone-2-carboxylate (7ag). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.1 Hz, 3H), 2.02−2.21 (m, 3H), 2.45−2.68 (m, 3H), 3.42 (d, J = 18.1 Hz, 1H), 3.75 (d, J = 18.2 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 7.12 (dd, J = 5.0 Hz, J = 3.8 Hz, 1H), 7.63 (dd, J = 4.9 Hz, J = 1.1 Hz, 1H), 7.73 (dd, J = 3.8 Hz, J = 1.2 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 13.9 (CH_3), 19.2 (CH_2), 33.3 (CH_2), 37.6 (CH_2), 43.6

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(CH_2), 57.4 (C), 61.7 (CH_2), 128.2 (CH), 132.3 (CH), 133.9 (CH), 143.4 (C), 170.5 (C), 189.7 (C), 214.8 (C) ppm. IR (ATR): λ^{-1} = 3106 (w), 3088 (w), 2977 (w), 2963 (w), 2917 (w), 1750 (s), 1722 (vs), 1662 (s), 1519 (w), 1447 (w), 1416 (s), 1360 (w), 1323 (w), 1263 (m), 1228 (s), 1191 (m), 1152 (m), 1103 (w), 1060 (w), 939 (w), 731 (m) cm^{-1}. HRMS (ESI): calcd. 303.0667 (for $C_{14}H_{16}NaO_4S^+$); found 303.0676 [M+Na^+]. $C_{14}H_{16}O_4S$ (280.34).

Ethyl 3-[2-Oxo-2-(2-furyl)ethyl]tetrahydropyran-2-one-3-carboxylate (11ah). $CeCl_3{\cdot}7\ H_2O$ (5 mg, 13 μmol) was added to a mixture of β-oxoester **5a** (201 mg, 1.28 mmol) and enol ester **8h** (253 mg, 1.66 mmol, 1.3 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 20 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 1:1 → 1:2) to yield the 1,4-diketone **7ah** [69 mg, 0.26 mmol, 20%, R_f = 0.29 (hexanes/MTBE 1:1)] as a colorless oil. Second, the title compound **11ah** [196 mg, 0.70 mmol, 55%, R_f = 0.08 (hexanes/MTBE 1:1)] was eluted as a light yellow oil.

Lactone 11ah. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.1 Hz, 3H), 1.81−1.87 (m, 1H), 2.12−2.20 (m, 3H), 3.47 (d, J = 18.5 Hz, 1H), 3.86 (d, J = 18.6 Hz, 1H), 4.18−4.29 (m, 2H), 4.50−4.53 (m, 1H), 4.59−4.65 (m, 1H), 6.53 (dd, J = 3.6 Hz, J = 1.7 Hz, 1H), 7.21 (d, J = 3.6 Hz, 1H), 7.57 (d, J = 1.7 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.0 (CH_2), 30.2 (CH_2), 45.0 (CH_2), 50.8 (C), 62.3 (CH_2), 69.9 (CH_2), 112.4 (CH), 117.6 (CH), 146.7 (CH), 152.0 (C), 169.6 (C), 171.2 (C), 185.7 (C) ppm. IR (ATR): λ^{-1} = 3131 (w), 2980 (w), 2938 (w), 1722 (vs), 1674 (s), 1571 (w), 1468 (s), 1399 (m), 1351 (w), 1281 (m), 1241 (m), 1200 (m), 1164 (m), 1120 (w), 1068 (w), 1021 (m), 985 (m), 883 (w), 857 (w), 770 (m), 637 (w) cm^{-1}. HRMS (ESI): calcd. 303.0840 (for $C_{14}H_{16}NaO_6^+$); found 303.0839 [M+Na^+]. $C_{14}H_{16}O_6$ (280.28).

Ethyl 2-[2-Oxo-2-(2-furyl)ethyl]cyclopentanone-2-carboxylate (7ah). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.1 Hz, 3H), 2.03−2.18 (m, 3H), 2.45−2.63 (m, 3H), 3.33 (d, J = 18.4 Hz, 1H), 3.67 (d, J = 18.4 Hz, 1H), 4.12−4.21 (m, 2H), 6.53 (dd, J = 3.5 Hz, J = 1.7 Hz, 1H), 7.19 (dd, J = 3.6 Hz, J = 0.7 Hz, 1H), 7.57 (dd, J = 1.7 Hz, J = 0.8 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.8 (CH_2), 33.3 (CH_2), 37.6 (CH_2), 42.7 (CH_2), 57.2 (C), 61.7 (CH_2), 112.3 (CH), 117.3 (CH), 146.5 (CH), 152.2 (C), 170.6 (C), 185.8 (C), 214.7 (C) ppm. IR (ATR): λ^{-1} = 2982 (w), 2909 (w), 1750 (s), 1724 (vs), 1679 (m), 1570 (w), 1469 (m), 1399 (w), 1368 (w), 1323 (w), 1278 (w), 1229 (m), 1158 (m), 1109 (w), 1019 (m), 769 (w), 634 (w) cm^{-1}. HRMS (ESI): calcd. 287.0892 (for $C_{14}H_{16}NaO_5^+$); found 287.0902 [M+Na^+]. $C_{14}H_{16}O_5$ (264.28).

Ethyl 3-{2-Oxo-2-[1-(4-methylphenylsulfonyl)pyrrol-2-yl]-ethyl}tetrahydropyran-2-one-3-carboxylate (11ai). $CeCl_3{\cdot}7\ H_2O$ (5 mg, 13 μmol) was added to a mixture of β-oxoester **5a** (200 mg, 1.28 mmol) and enol ester **8i** (507 mg, 1.66 mmol, 1.3 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 22 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 3:1 → 1:1) to yield the α-hydroxylated compound **10a** [53 mg, 0.31 mmol, 24%, R_f = 0.31 (hexanes/MTBE 1:1)] as a colorless oil. Second, the 1,4-diketone **7ai** [87 mg, 0.21 mmol, 16%, R_f = 0.27 (hexanes/MTBE 1:1)]) was obtained as a colorless oil. As a third fraction the title compound **11ai** [201 mg, 0.46 mmol, 36%, R_f = 0.10 (hexanes/MTBE 1:1)] was eluted as a yellow oil.

Lactone 11ai. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.2 Hz, 3H), 1.75−1.82 (m, 1H), 2.00−2.19 (m, 3H), 2.38 (s, 3H), 3.33 (d, J = 17.9 Hz, 1H), 3.70 (d, J = 17.9 Hz, 1H), 4.09−4.28 (m, 2H), 4.45−4.60 (m, 2H), 6.30 (dd, J = 3.7 Hz, J = 3.2 Hz, 1H), 7.08 (dd, J = 3.8 Hz, J = 1.7 Hz, 1H), 7.25−7.28 (m, 2H), 7.75 (dd, J = 3.2 Hz, J = 1.7 Hz, 1H), 7.82−7.86 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 13.9 (CH_3), 21.0 (CH_2), 21.6 (CH_3), 30.0 (CH_2), 45.7 (CH_2), 51.0 (C), 62.2 (CH_2), 69.8 (CH_2), 110.4 (CH), 123.8 (CH), 128.4 (2 CH), 129.3 (2 CH), 130.3 (CH), 132.4 (C), 135.3 (C), 145.0 (C), 169.5 (C), 171.1 (C), 184.8 (C) ppm. IR (ATR): λ^{-1} = 2984 (w), 2946 (w), 1724 (vs), 1675 (m), 1596 (w), 1439 (w), 1405 (m), 1364 (w), 1304 (w), 1245 (m), 1171 (s), 1143 (m), 1090 (m), 1020 (w), 815 (m), 736 (m), 670 (s) cm^{-1}. HRMS (ESI): calcd. 456.1088 (for $C_{21}H_{23}NNaO_7S^+$); found 456.1087 [M+Na^+]. $C_{21}H_{23}NO_7S$ (433.48).

Ethyl 2-{2-Oxo-2-[1-(4-methylphenylsulfonyl)pyrrol-2-yl]-ethyl}cyclopentanone-2-carboxylate (7ai). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, J = 7.1 Hz, 3H), 1.92−2.16 (m, 3H), 2.36−2.47 (m, 2H), 2.40 (s, 3H), 2.50−2.58 (m, 1H), 3.13 (d, J = 17.7 Hz, 1H), 3.52 (d, J = 17.7 Hz, 1H), 3.98−4.13 (m, 2H), 6.31 (dd, J = 3.7 Hz, J = 3.2 Hz, 1H), 7.06 (dd, J = 3.8 Hz, J = 1.7 Hz, 1H), 7.24−7.31 (m, 2H), 7.76 (dd, J = 3.2 Hz, J = 1.7 Hz, 1H), 7.81−7.86 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 13.9 (CH_3), 19.8 (CH_2), 21.6 (CH_3), 33.2 (CH_2), 37.7 (CH_2), 43.5 (CH_2), 57.5 (C), 61.6 (CH_2), 110.4 (CH), 123.6 (CH), 128.5 (2 CH), 129.2 (2 CH), 130.2 (CH), 132.6 (C), 135.6 (C), 144.9 (C), 170.4 (C), 184.8 (C), 214.6 (C) ppm. IR (ATR): λ^{-1} = 2977 (w), 2930 (w), 1748 (s), 1721 (vs), 1678 (m), 1596 (w), 1439 (m), 1403 (m), 1365 (m), 1228 (w), 1172 (vs), 1143 (vs), 1091 (m), 1016 (m), 953 (w), 856 (w), 814 (m), 755 (m), 671 (s) cm^{-1}. HRMS (ESI): calcd. 440.1138 (for $C_{21}H_{23}NNaO_6S^+$); found 440.1155 [M+Na^+]. $C_{21}H_{23}NO_6S$ (417.48).

Isobutyl 3-(2-Oxo-2-phenylethyl)tetrahydropyran-2-one-3-carboxylate (11ba). $CeCl_3{\cdot}7\ H_2O$ (5 mg, 13 μmol) was added to a mixture of β-oxoester **5b** (221 mg, 1.20 mmol) and enol ester **8a** (389 mg, 2.40 mmol, 2.0 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 2:1) to yield 1,4-diketone **7ba** (106 mg, 0.35 mmol, 29%, R_f = 0.34) as a colorless oil. Second, the α-hydroxylated compound **10b** (16 mg, 0.08 mmol, 7%, R_f = 0.23) was eluted as a colorless oil. As a third fraction the title compound **11ba** (244 mg, 0.77 mmol, 64%, R_f = 0.14) was eluted as a colorless oil.

Lactone 11ba. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 1.84−1.89 (m, 1H), 1.97 (nonet, J = 6.7 Hz, 1H), 2.10−2.24 (m, 3H), 3.62 (d, J = 18.6 Hz, 1H), 3.93−4.00 (m, 2H), 4.03 (d, J = 18.6 Hz, 1H), 4.52−4.56 (m, 1H), 4.67−4.72 (m, 1H), 7.42−7.45 (m, 2H), 7.54−7.57 (m, 1H), 7.93−7.95 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 18.9 (2 CH_3), 21.0 (CH_2), 27.6 (CH), 30.23 (CH_2), 45.7 (CH_2), 51.0 (C), 69.9 (CH_2), 72.1 (CH_2), 128.0 (2 CH), 128.5 (2 CH) 133.6 (CH), 136.0 (C), 169.7 (C), 171.5 (C), 196.7 (C) ppm. IR (ATR): λ^{-1} = 2965 (w), 2936 (w), 2878 (w), 1724 (vs), 1686 (s), 1599 (w), 1452 (m), 1407 (m), 1356 (m), 1284 (m), 1252 (s), 1219 (m), 1200 (s), 1170 (m), 1121 (m), 1003 (m), 988 (m), 945 (w), 756 (m), 692 (m), 642 (w) cm^{-1}. HRMS (ESI): calcd. 319.1540 (for $C_{18}H_{23}O_5^+$); found 319.1558 [M+H^+]. $C_{18}H_{22}O_5$ (318.37).

Isobutyl 2-(2-Oxo-2-phenylethyl)cyclopentanone-2-carboxylate (7ba). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 (d, J = 6.8 Hz, 6H), 1.92 (nonet, J = 6.6 Hz, 1H), 2.06−2.23 (m, 3H), 2.52 (dddd, J = 18.6 Hz, J = 8.5 Hz, J = 3.6 Hz, J = 1.0 Hz, 1H), 2.60−2.67 (m, 2H), 3.49 (d, J = 18.6 Hz, 1H), 3.85 (d, J = 18.5 Hz, 1H), 3.90 (d, J = 6.5 Hz, 2H), 7.43−7.46 (m, 2H), 7.55−7.58 (m, 1H), 7.93−7.95 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 19.0 (2 CH_3), 19.9 (CH_2), 27.7 (CH), 33.4 (CH_2), 37.7 (CH_2), 43.5 (CH_2), 57.4 (C), 71.6 (CH_2), 128.0 (2 CH), 128.6 (2 CH), 133.4 (CH), 136.3 (C), 170.8 (C), 196.7 (C), 214.9 (C) ppm. IR (ATR): λ^{-1} = 2962 (m), 2875 (w), 1751 (s), 1722 (vs), 1689 (vs), 1597 (w), 1470 (w), 1449 (m), 1402 (w), 1354 (m), 1260 (m), 1221 (vs), 1152 (m), 1106 (m), 1027 (w), 991 (m), 922 (w), 753 (s), 690 (m) cm^{-1}. HRMS (ESI): calcd. 303.1591 (for $C_{18}H_{23}O_4^+$); found 303.1588 [M+H^+]. $C_{18}H_{22}O_4$ (302.37).

Isobutyl 2-Hydroxycyclopentanone-2-carboxylate (10b). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (d, J = 6.7 Hz, 6H), 1.96 (nonet, J = 6.7 Hz, 1H), 2.07−2.16 (m, 3H), 2.42−2.54 (m, 3H), 3.67 (s, 1H), 3.95−4.04 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 18.4 (CH_2), 18.9 (2 CH_3), 27.7 (CH), 34.8 (CH_2), 35.8 (CH_2), 72.4 (CH_2), 79.8 (C), 171.6 (C), 213.3 (C) ppm. IR (ATR): λ^{-1} = 3481 (m), 2966 (m), 2878 (w), 1758 (s), 1731 (vs), 1472 (m), 1373 (m), 1257 (m), 1166 (s), 1100 (m), 1051 (m), 1010 (m), 984 (m), 946 (m), 917 (m), 823 (w), 786 (w) cm^{-1}. GCMS (EI, 70 eV): m/z (%)

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200 (0.5) [M^+], 144 (27) [$M^+ - C_4H_8$], 88 (82) [$M^+ - C_6H_8O_2$], 57 (100) [$M^+ - C_6H_8O_4$]. $C_{10}H_{16}O_4$ (200.23).

Isobutyl 3-[2-Oxo-2-(4-methoxyphenyl)ethyl]-tetrahydropyran-2-one-3-carboxylate (11bc). $CeCl_3 \cdot 7\ H_2O$ (5 mg, 13 μmol) was added to a mixture of β-oxoester **5b** (220 mg, 1.20 mmol) and enol ester **8c** (346 mg, 1.80 mmol, 1.5 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 1:1) to yield 1,4-diketone **7bc** (83 mg, 0.25 mmol, 21%, R_f = 0.42) as a colorless oil. Second, the α-hydroxylated compound **10b** (5 mg, 0.02 mmol, 2%, R_f = 0.36) was eluted as a colorless oil. As a third fraction the title compound **11bc** (309 mg, 0.89 mmol, 74%, R_f = 0.22) was eluted as a light yellow oil.

Lactone 11bc. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 1.82−1.87 (m, 1H), 1.97 (nonet, J = 6.7 Hz, 1H), 2.07−2.23 (m, 3H), 3.57 (d, J = 18.3 Hz, 1H), 3.84 (s, 3H), 3.96−4.00 (m, 2H), 3.98 (d, J = 18.4 Hz, 1H), 4.51−4.56 (m, 1H), 4.66−4.72 (m, 1H), 6.89−6.92 (m, 2H), 7.90−7.93 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 18.9 (CH_3), 19.0 (CH_3), 21.1 (CH_2), 27.6 (CH), 30.3 (CH_2), 45.4 (CH_2), 51.0 (C), 55.4 (CH_3), 69.9 (CH_2), 72.1 (CH_2), 113.7 (2 CH), 129.2 (C), 130.3 (2 CH), 163.8 (C), 169.8 (C), 171.6 (C), 195.1 (C) ppm. IR (ATR): λ^{-1} = 2964 (w), 2936 (w), 2876 (w), 2843 (w), 1739 (s), 1723 (vs), 1673 (m), 1601 (vs), 1575 (w), 1511 (w), 1470 (w), 1407 (w), 1353 (w), 1251 (s), 1223 (m), 1169 (vs), 1118 (m), 1029 (w), 998 (m), 831 (m), 640 (w) cm^{-1}. HRMS (ESI): calcd. 349.1646 (for $C_{19}H_{25}O_6^+$); found 349.1644 [M+H$^+$]. $C_{19}H_{24}O_6$ (348.40).

Isobutyl 2-[2-Oxo-2-(4-methoxyphenyl)ethyl]-cyclopentanone-2-carboxylate (7bc). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 (d, J = 6.8 Hz, 6H), 1.91 (nonet, J = 6.7 Hz, 1H), 2.05−2.21 (m, 3H), 2.50 (dddd, J = 18.8 Hz, J = 8.8 Hz, J = 3.9 Hz, J = 1.2 Hz, 1H), 2.59−2.67 (m, 2H), 3.46 (d, J = 18.4 Hz, 1H), 3.80 (d, J = 18.4 Hz, 1H), 3.85 (s, 3H), 3.89 (d, J = 6.5 Hz, 2H), 6.90−6.92 (m, 2H), 7.89−7.92 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 19.0 (2 CH_3), 19.8 (CH_2), 27.7 (CH), 33.4 (CH_2), 37.7 (CH_2), 43.2 (CH_2), 55.5 (CH_3), 57.4 (C), 71.6 (CH_2), 113.7 (2 CH), 129.4 (C), 130.3 (2 CH), 164.7 (C), 170.9 (C), 195.2 (C), 215.1 (C) ppm. IR (ATR): λ^{-1} = 2962 (m), 2876 (w), 1751 (s), 1722 (vs), 1677 (m), 1601 (vs), 1576 (w), 1511 (w), 1468 (w), 1403 (w), 1354 (w), 1259 (s), 1225 (s), 1169 (vs), 1112 (m), 1028 (w), 988 (m), 833 (m) cm^{-1}. HRMS (ESI): calcd. 333.1697 (for $C_{19}H_{25}O_5^+$); found 333.1693 [M+H$^+$]. $C_{19}H_{24}O_5$ (332.40).

Ethyl 3-(2-Oxo-2-phenylethyl)oxepan-2-one-3-carboxylate (11ca). $CeCl_3 \cdot 7\ H_2O$ (5 mg, 13 μmol) was added to a mixture of β-oxoester **5c** (209 mg, 1.23 mmol) and enol ester **8a** (300 mg, 1.85 mmol, 1.5 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 3:1 → 1:1) to yield the 1,4-diketone **7ca** [147 mg, 0.51 mmol, 41%, R_f = 0.41 (hexanes/MTBE 1:1)] as a colorless solid (mp 89 °C). Second, the α-hydroxylated compound **10c** [21 mg, 0.11 mmol, 9%, R_f = 0.33 (hexanes/MTBE 1:1)]) was obtained as a colorless oil. As a third fraction the title compound **11ca** [35 mg, 0.12 mmol, 9%, R_f = 0.16 (hexanes/MTBE 1:1)] was eluted as a colorless solid (mp 105 °C).

Lactone 11ca. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.2 Hz, 3H), 1.66−1.94 (m, 4H), 2.06 (ddd, J = 14.6 Hz, J = 12.6 Hz, J = 2.7 Hz, 1H), 2.21−2.25 (m, 1H), 3.35 (d, J = 16.7 Hz, 1H), 3.71 (d, J = 16.7 Hz, 1H), 4.28−4.35 (m, 3H), 4.43−4.48 (m, 1H), 7.42−7.45 (m, 2H), 7.52−7.55 (m, 1H), 7.92−7.94 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 14.1 (CH_3), 24.7 (CH_2), 28.4 (CH_2), 33.5 (CH_2), 47.8 (CH_2), 58.5 (C), 62.1 (CH_2), 69.4 (CH_2), 128.1 (2 CH), 128.5 (2 CH), 133.1 (CH), 136.9 (C), 170.8 (C), 172.1 (C), 196.5 (C) ppm. IR (ATR): λ^{-1} = 2975 (w), 2936 (w), 2919 (m), 2861 (w), 1721 (s), 1704 (vs), 1691 (vs), 1598 (w), 1467 (m), 1451 (m), 1395 (w), 1328 (m), 1251 (w), 1206 (vs), 1178 (s), 1169 (m), 1131 (m), 1092 (m), 1021 (m), 1002 (m), 958 (w), 860 (w), 848 (w), 768 (m), 693 (s), 619 (s), 572 (w) cm^{-1}. HRMS (ESI): calcd. 327.1203 (for $C_{17}H_{20}NaO_5^+$); found 327.1197 [M+Na$^+$]. $C_{17}H_{20}O_5$ (304.34).

Ethyl 2-(2-Oxo-2-phenylethyl)cyclohexanone-2-carboxylate (7ca). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3H), 1.74−1.85 (m, 4H), 2.04−2.09 (m, 1H), 2.44−2.48 (m, 1H), 2.49−2.54 (m, 1H), 2.83 (ddd, J = 14.5 Hz, J = 12.9 Hz, J = 6.4 Hz, 1H), 3.37 (d, J = 17.4 Hz, 1H), 3.55 (d, J = 17.4 Hz, 1H), 4.17−4.27 (m, 2H), 7.42−7.45 (m, 2H), 7.52−7.56 (m, 1H), 7.93−7.95 (m, 2H) ppm. The data were in accordance with literature values.[12]

Ethyl 2-Hydroxycyclohexanone-2-carboxylate (10c). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26 (t, J = 7.1 Hz, 3H), 1.61−1.86 (m, 4H), 2.00−2.03 (m, 1H), 2.50−2.67 (m, 3H), 4.21 (q, J = 7.1 Hz, 2H), 4.33 (s, 1H) ppm. The data were in accordance with literature values.[13b]

Methyl 2-(2-Oxo-2-phenylethyl)cycloheptanone-2-carboxylate (7da). $CeCl_3 \cdot 7\ H_2O$ (5 mg, 13 μmol) was added to a mixture of β-oxoester **5d** (209 mg, 1.23 mmol) and enol ester **8a** (301 mg, 1.85 mmol, 1.5 equiv) in TFE (1 mL), and the reaction mixture was stirred at 30 °C for 24 h under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 2:1) to yield the 1,4-diketone **7da** (158 mg, 0.55 mmol, 45%, R_f = 0.26) as a colorless oil. As a second fraction the α-hydroxylated compound **10d** (9 mg, 0.05 mmol, 4%, R_f = 0.21) was obtained as a colorless oil.

1,4-Diketone 7da. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.29 (dt, J = 13.8 Hz, J = 9.8 Hz, 1H), 1.48−1.61 (m, 2H), 1.66−1.75 (m, 2H), 1.78−1.87 (m, 1H), 2.10 (dd, J = 15.1 Hz, J = 9.4 Hz, 1H), 2.29 (dd, J = 15.1 Hz, J = 10.2 Hz, 1H), 2.56 (ddd, J = 12.3 Hz, J = 8.3 Hz, J = 2.4 Hz, 1H), 2.87 (ddd, J = 13.6 Hz, J = 11.0 Hz, J = 2.7 Hz, 1H), 3.26 (d, J = 17.7 Hz, 1H), 3.70 (s, 3H), 3.84 (d, J = 17.7 Hz, 1H), 7.40−7.45 (m, 2H), 7.51−7.54 (m, 1H), 7.92−7.95 (m, 2H) ppm. The data were in accordance with literature values.[12]

Methyl 2-Hydroxycycloheptanone-2-carboxylate (10d). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25−1.33 (m, 1H), 1.39−1.49 (m, 2H), 1.74−1.82 (m, 2H), 1.88−1.95 (m, 1H), 2.06 (dd, J = 15.0 Hz, J = 8.0 Hz, 1H), 2.22 (dd, J = 14.9 Hz, J = 10.8 Hz, 1H), 2.54 (ddd, J = 11.7 Hz, J = 7.2 Hz, J = 2.2 Hz, 1H), 2.90 (ddt, J = 12.1 Hz, J = 9.0 Hz, J = 2.8 Hz, 1H), 3.71 (s, 3H), 4.28 (s, 1H) ppm. The data were in accordance with literature values.[13b]

3-Acetyl-3-(2-oxo-2-phenylethyl)tetrahydro-2-pyranone (11ea). $CeCl_3 \cdot 7\ H_2O$ (4 mg, 11 μmol) was added to a mixture of β-oxoester **5e** (126 mg, 1.00 mmol) and enol ester **8a** (178 mg, 1.10 mmol, 1.1 equiv) in TFE (1 mL), and the reaction mixture was stirred at 50 °C for 3 d under an atmosphere of air. Subsequently, all volatile materials were removed in vacuum and the residue was purified by column chromatography (SiO_2, hexanes/MTBE 1:2) to yield the 1,4-diketone **7ea** (58 mg, 0.24 mmol, 24%, R_f = 0.42) as a colorless oil. As a second fraction the title compound **11ea** (36 mg, 0.14 mmol, 14%, R_f = 0.19) was eluted as a colorless oil.

Lactone 11ea. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.85−2.04 (m, 3H), 2.29−2.34 (m, 1H), 2.37 (s, 3H), 3.45 (d, J = 18.2 Hz, 1H), 3.91 (d, J = 18.3 Hz, 1H), 4.50−4.54 (m, 1H), 4.65−4.70 (m, 1H), 7.45−7.48 (m, 2H), 7.57−7.60 (m, 1H), 7.93−7.95 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 21.7 (CH_2), 27.4 (CH_3), 28.7 (CH_2), 45.8 (CH_2), 57.7 (C), 70.3 (CH_2), 128.1 (2 CH), 128.7 (2 CH), 133.8 (CH), 136.0 (C), 171.6 (C), 196.3 (C), 204.8 (C) ppm. IR (ATR): λ^{-1} = 3064 (w), 2971 (w), 2922 (w), 1731 (m), 1705 (s), 1685 (vs), 1599 (w), 1582 (w), 1451 (m), 1406 (w), 1355 (m), 1299 (w), 1283 (m), 1225 (m), 1163 (m), 1113 (w), 1004 (w), 980 (w), 757 (m), 693 (m), 632 (w) cm^{-1}. HRMS (ESI): calcd. 283.0941 (for $C_{15}H_{16}NaO_4^+$); found 283.0937 [M+Na$^+$]. $C_{15}H_{16}O_4$ (260.29).

2-Acetyl-2-(2-oxo-2-phenylethyl)cyclopentanone (7ea). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.88 (dt, J = 13.4 Hz, J = 8.7 Hz, 1H), 2.00−2.07 (m, 2H), 2.20 (s, 3H), 2.42 (ddd, J = 18.9 Hz, J = 7.6 Hz, J = 5.8 Hz, 1H), 2.55 (dt, J = 18.7 Hz, J = 9.3 Hz, 1H), 2.82 (ddd, J = 13.7 Hz, J = 6.3 Hz, J = 4.7 Hz, 1H), 3.49 (d, J = 18.5 Hz, 1H), 3.79 (d, J = 18.4 Hz, 1H), 7.44−7.48 (m, 2H), 7.56−7.60 (m, 1H), 7.90−7.94 (m, 2H) ppm. The data were in accordance with literature values.[11c]

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01441.

Copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of all reported products, details on single crystal X-ray structure determination as well as ORTEP plots of compounds **7ab** and **11ab**, and screening results of other metal salts as precatalysts in the title reaction (PDF)

X-ray crystallographic data for **7ab** (CIF)

X-ray crystallographic data for **11ab** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: jens.christoffers@uni-oldenburg.de

Notes

The authors declare no competing financial interest.

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(18) CCDC 1476570 (**11ab**) and 1476571 (**7ab**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: + 44 1223 336033.

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