Five roads that converge at the cyclic peroxy-Criegee intermediates: BF_3-catalyzed synthesis of β-hydroperoxy- β-peroxylactones

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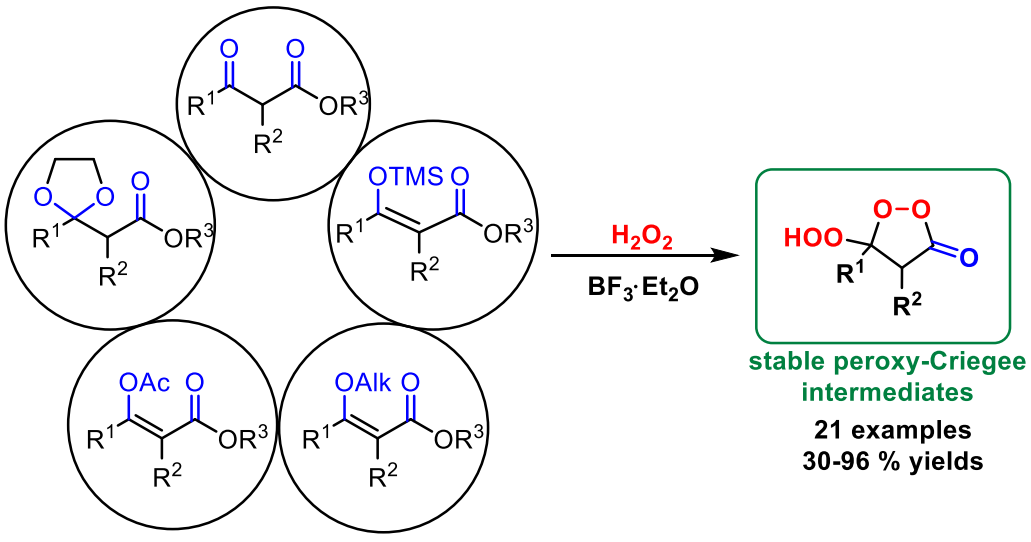


ABSTRACT. We have discovered synthetic access to β-hydroperoxy-β-peroxylactones *via* BF_3-catalyzed cyclizations of a variety of acyclic precursors, β-ketoesters and their silyl enol ethers, alkyl enol ethers, enol acetates, and cyclic acetals, with H_2O_2. Strikingly, independent on the choice of starting material, these reactions converge at the same β-hydroperoxy-β-peroxylactone products, i.e., the peroxy analogs of the previously elusive cyclic Criegee intermediate of the Baeyer-Villiger reaction. Computed thermodynamic parameters for the formation of the β-hydroperoxy-β-peroxylactones from silyl enol ethers, enol acetates, and cyclic acetals confirm that the β-peroxylactones indeed correspond to a deep energy minimum that connects a variety of the interconverting oxygen-rich species at this combined potential energy surface. The target β-hydroperoxy-β-peroxylactones were synthesized from β-ketoesters, and their silyl enol ethers, alkyl enol ethers, enol acetates, and cyclic acetals in 30-96% yields. These reactions proceed under mild conditions and open synthetic access to a broad selection of β-hydroperoxy-β-peroxylactones that are formed selectively even in those cases when alternative oxidation pathways can be expected. These β-peroxylactones are stable and can be useful for further synthetic transformations.

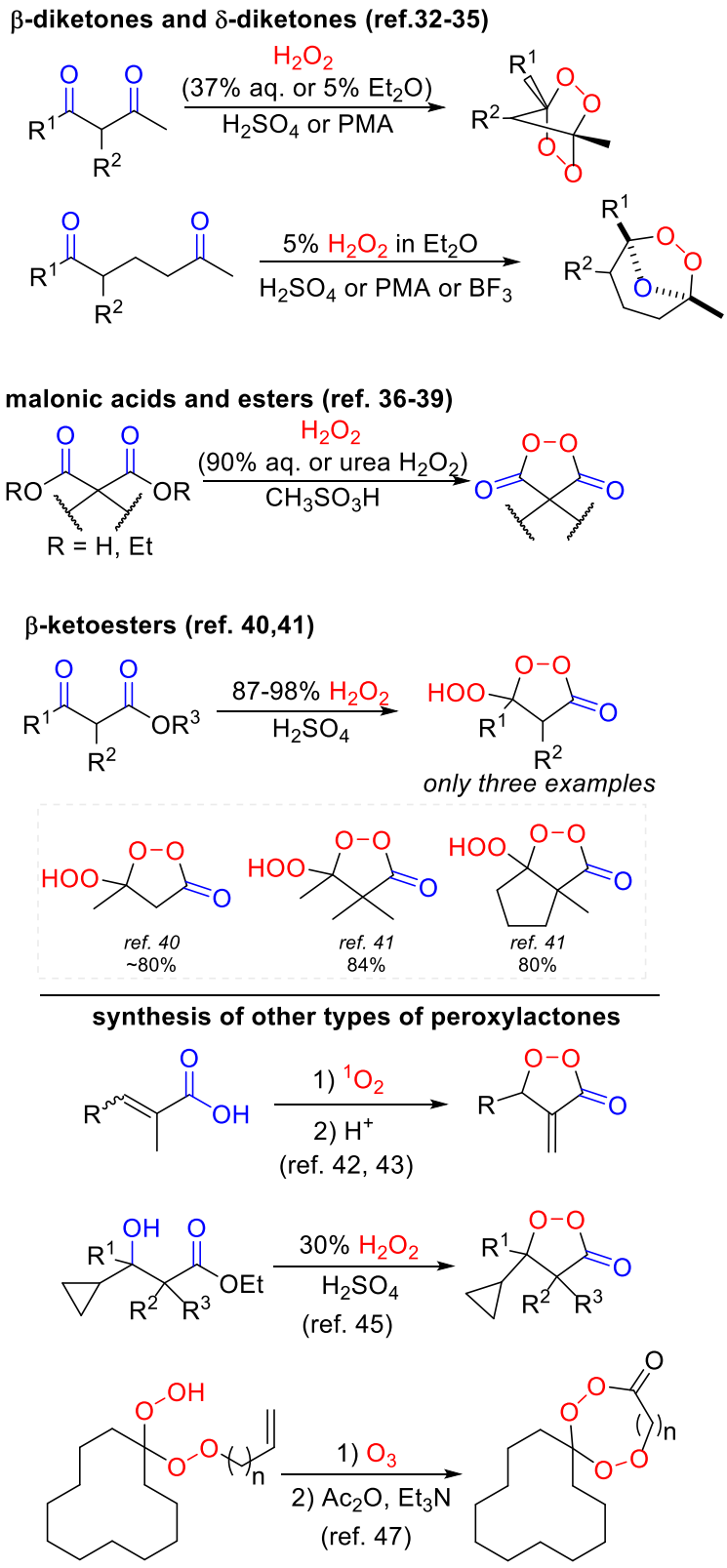
Keywords Baeyer-Villiger reaction, peroxides, dicarbonyl compounds, peroxidation, boron trifluoride

INTRODUCTION

The recent surge of research in the chemistry of cyclic organic peroxides stems from the discovery of the potent antimalarial,[1-3] anthihelmintic,[4,5] cytotoxic,[6] fungicide,[7,8] and antiviral[9,10] activities. The key role of natural peroxide artemisinin and its derivatives in the treatment of malaria in the last decades was recognized by a Nobel Prize in Medicine in 2015.[11-13] While

searching for synthetically available and affordable peroxides, it was shown that 5- and 6-membered cyclic peroxides display a broad spectrum of biological activity.[14-16] It is now apparent that cyclic organic peroxides, that used to be considered exotic and dangerous compounds of minor importance, can lead to breakthroughs in medicinal chemistry. Consequently, the development of selective synthetic approaches to these compounds became an important problem for modern organic chemistry.

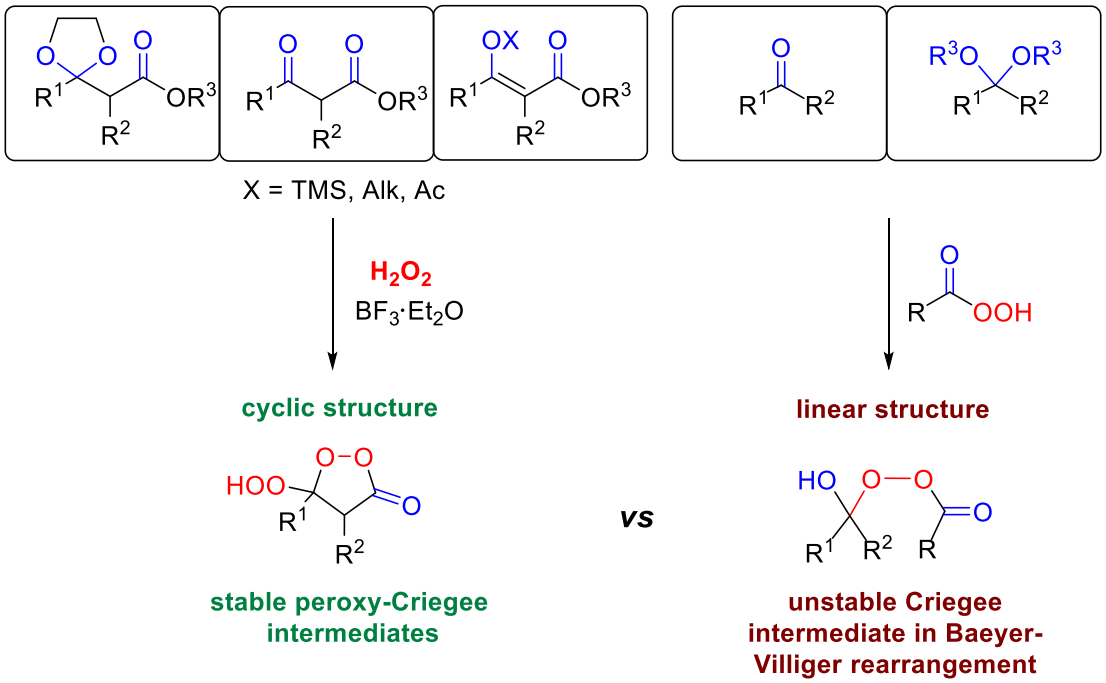
Currently, the reaction of ketones or aldehydes with H_2O_2 and hydroperoxides serve as one of the main synthetic approaches to organic peroxides.[17-21] Although many publications describe reactions of hydrogen peroxide and monoketones,[22-27] the problem of peroxidation selectivity in the presence of several reactive centers has not found a general solution. For β-dicarbonyl compounds, this issue has been successfully addressed only in a small number of literature reports.[28-31] It was shown that β-diketones can be transformed into 1,2,4,5-tetraoxanes [32,33] whereas δ-diketones can be converted in 1,2,4-trioxolanes (ozonides) (Scheme 1).[34,35] Peroxidation of malonic acids and their esters yields malonyl peroxides (Scheme 1).[36-39] In this context, peroxidation of β-ketoesters is potentially challenging because of the large difference in the reactivity of ketone and ester groups towards hydrogen peroxide. The only two earlier reports described the formation of β-hydroperoxy-β-peroxylactones from the simplest β-ketoesters, the acetoacetic ester, and two α,α-disubstituted β-ketoesters[40,41] by using the explosive concentrated hydrogen peroxide (87-90%) (Scheme 1).



Scheme 1. Selection of known methods of peroxidation of dicarbonyl compounds and synthesis of peroxylactones.

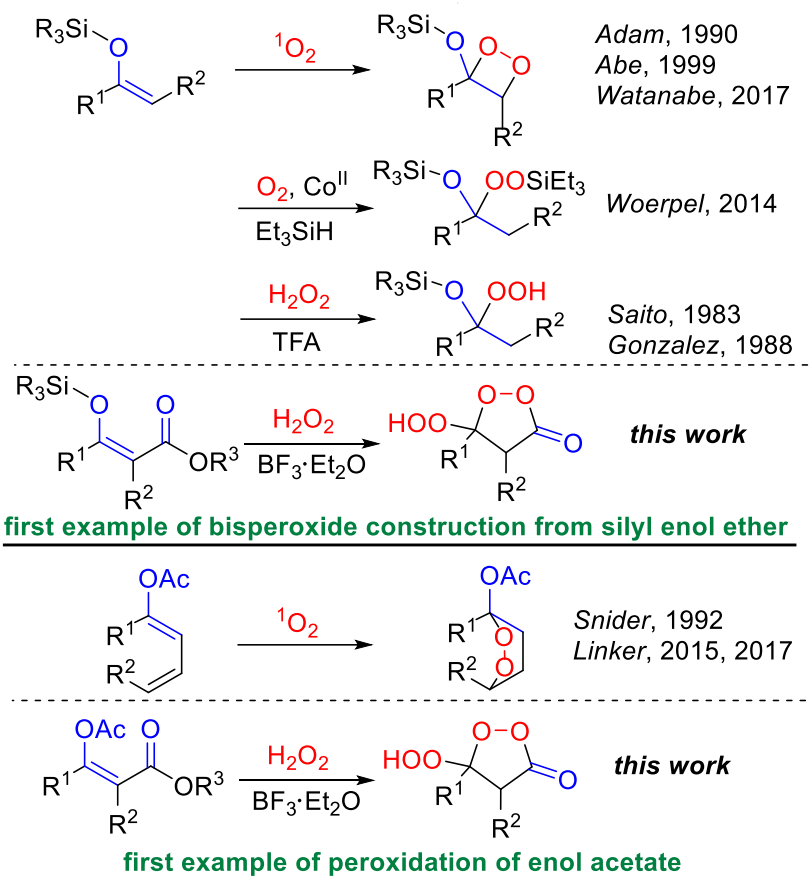
On the other hand, the related β-peroxylactones were obtained in several other ways (Scheme1) that include photooxidation of α,β-unsaturated carboxylic acids with the subsequent acid-catalyzed cyclization,[42,43] photolysis of lactone with (diacetoxyiodo)-benzene (DIB) and iodine under oxygen atmosphere,[44] and treatment of β-hydroxy esters with H_2O_2 in the presence of H_2SO_4.[45] α-Keto-β-peroxylactone is considered to be an intermediate in oxidation of p-methoxyphenylpyruvic acid by oxygen.[46] Ozonolysis of (alkenyldioxy)cyclododecyl hydroperoxides in CF_3CH_2OH with subsequent dehydration of the hydroperoxides [47] or reaction of epoxyketones with H_2O_2[48,49] are other possible synthetic routes to peroxylactones. Although these approaches have synthetic value, they lack simplicity and affordability associated with the use of dicarbonyl compounds and hydrogen peroxide as starting materials.

We have recently reported[50] that β-hydroxy-β-peroxylactones, the stable cyclic Criegee intermediates[51] constrained within a five-membered ring, can be prepared by mild reduction of respective hydroperoxyl peroxyesters (β-hydroperoxy-β-peroxylactones). This discovery is based on convenient and efficient BF_3-mediated synthesis of these bisperoxides from β-ketoesters and H_2O_2. In this work, we disclose substantial study of discovered reaction, investigate scope of the new transformation, and complement it with expanded computational analysis that compared energy profiles for the alternative pathways. We also explored additional transformations of β-hydroperoxy-β-peroxylactones with the goal to evaluate the stability of bisperoxide moiety and measured oxidative properties of the new β-peroxylactones with cyclic voltammetry. An important fundamental finding of the study is that the target peroxides can be also obtained from silyl enol ethers, alkyl enol ethers, enol acetates, and cyclic acetals (Scheme 2). This finding substantially expands the choice of practical approaches to such cyclic peroxides. Remarkably, the β-hydroperoxy-β-peroxylactones are obtained from enol ethers and acetals despite the presence of possible oxidative transformations.[52-55]



Scheme 2. The stable and unstable peroxides from di- and monocarbonyl compounds, respectively.

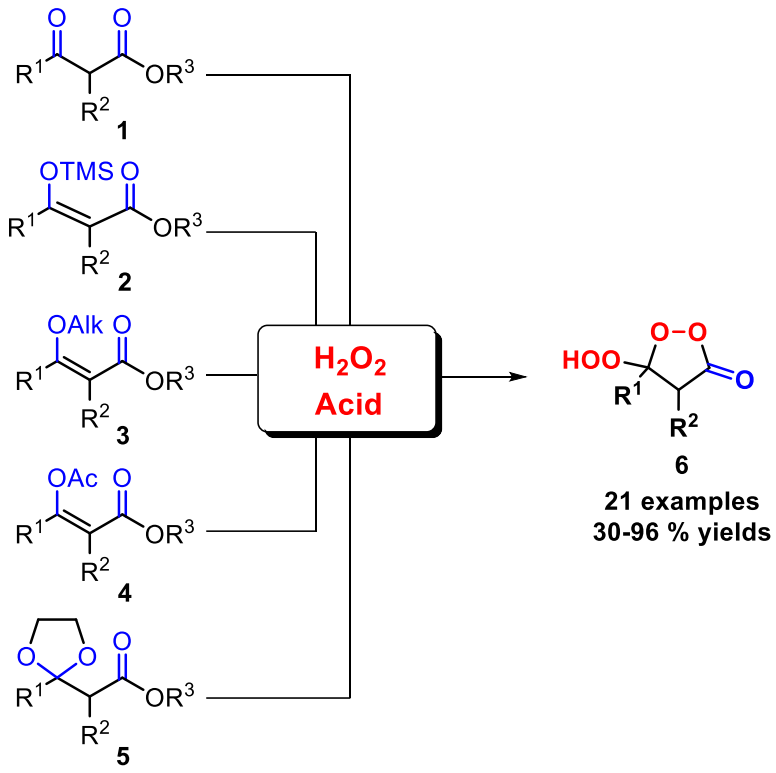
To the best of our knowledge, there are few reports describing peroxidation of silyl enol ethers, alkyl enol ethers,[56] enol acetates and acetals[57-59]. A literature search shows that only mono peroxy-compounds were prepared from silyl enol ethers,[60-65] but bisperoxide synthesis was not described (Scheme 3). Peroxides from enol acetates were prepared exclusively by photooxygenation of α-acetoxy diene compounds (Scheme 3).[66-68] In this paper, we disclose bisperoxidation of silyl enol ethers, alkyl enol ethers, enol acetates and acetals with additional ester group accompanied intermolecular cyclization between hydroperoxyl fragment and ester group (Scheme 3).



Scheme 3. Peroxidation of silyl enol ethers and enol acetates.

RESULTS AND DISCUSSION

Our goal was to develop a convenient and selective single step access to β-hydroperoxy-β-peroxylactones **6** via BF_3-catalyzed cyclizations of a variety of acyclic precursors, β-ketoesters **1** and their silyl enol ethers **2**, alkyl enol ethers **3**, enol acetates **4**, cyclic acetals **5**, with H_2O_2 (Scheme 4). We have concentrated on the use of boron trifluoride as the peroxidation catalyst[69] because this catalyst was shown to work well in earlier synthesis of bishydroperoxides, [58] 1,1′-bishydroperoxydi(cycloalkyl) peroxides,[70] and 1,2,4-trioxanes,[71,72] as well as various peroxides from acetals and enol ethers.[56]

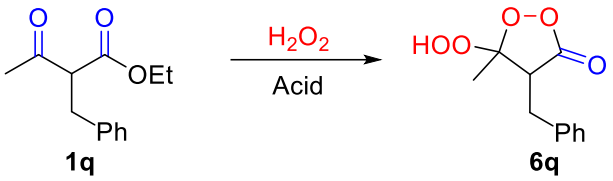


1a, **3a**: R^1 = CH_3, R^2 = H, R^3 = CH_2CH_3, Alk = CH_2CH_3; **1b**, **2b**: R^1 = $CH_2CH_2CH_3$, R^2 = H, R^3 = CH_2CH_3;
1c: R^1 = $CH(CH_3)_2$, R^2 = H, R^3 = CH_2CH_3; **1d**: R^1 = $CH_2CH(CH_3)_2$, R^2 = H, R^3 = CH_2CH_3;
1e, 2e: R^1 = $CH_2C(O)OCH_3$, R^2 = H, R^3 = CH_3; **1f**: R^1 = $CH_2C(O)OCH_2CH_3$, R^2 = H, R^3 = CH_2CH_3;
1g, 3g, 4g: R^1 = Ph, R^2 = H, R^3 = CH_2CH_3, Alk = 1,4-dioxan-2-yl; **1h**: R^1 = CH_2Ph, R^2 = H, R^3 = CH_2CH_3;
1i: R^1,R^2 = -$(CH_2)_3$-, R^3 = CH_2CH_3; **1j, 5j**: R^1,R^2 = -$(CH_2)_4$-, R^3 = CH_2CH_3;
1k: R^1 = CH_3, R^2 = Ad, R^3 = CH_2CH_3; **1l**: R^1 = CH_3, R^2 = CH_2CCH, R^3 = CH_2CH_3;
1m: R^1 = CH_3, R^2 = $CH_2C(O)OCH_2CH_3$, R^3 = CH_2CH_3;
1n, 4n: R^1 = CH_3, R^2 = $CH_2CH_2C(O)OCH_2CH_3$, R^3 = CH_2CH_3;
1o, 5o: R^1 = CH_3, R^2 = CH_2CH_2CN, R^3 = CH_2CH_3; **1p**: R^1 = CH_3, R^2 = $CH_2CH_2C(O)CH_3$, R^3 = CH_2CH_3;
1q, 2q, 3q, 4q, 5q: R^1 = CH_3, R^2 = CH_2Ph, R^3 = CH_2CH_3, Alk = 1,4-dioxan-2-yl;
1r: R^1 = CH_3, R^2 = CH_2(4-$(CH_3)_3C$-C_6H_4), R^3 = CH_2CH_3; **1s**: R^1 = CH_3, R^2 = CH_2(4-Cl-C_6H_4), R^3 = CH_2CH_3;
1t: R^1 = CH_3, R^2 = CH_2(4-Br-C_6H_4), R^3 = $C(CH_3)_3$; **1u**: R^1 = $CH_2CH_2CH_3$, R^2 = CH_2Ph, R^3 = CH_2CH_3;

Scheme 4. Synthesis of β-hydroperoxy-β-peroxylactones **6a-u** from β-ketoesters **1a-u**, silyl enol ethers **2b, 2e, 2q**, alkyl enol ethers **3a, 3g, 3q**, enol acetates **4g, 4n, 4q**, cyclic acetals **5j, 5o, 5q**, and hydrogen peroxide.

The optimization of synthetic procedures for the preparation of β-hydroperoxy-β-peroxylactones **6** was carried out for 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one **6q**, obtained from ethyl 2-benzyl-3-oxobutanoate **1q** due to convenience of analysis of **6q**. In particular, we determined the effect of acid type and concentration, as well as the amount of hydrogen peroxide on the yield of β-peroxylactone **6q** (Table 1).

Table 1. Optimization of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one **6q** synthesis from ethyl 2-benzyl-3-oxobutanoate **1q** and H_2O_2.[a]



1q **6q**

Entry	H_2O_2 (type, equiv.)[b]	Acid (equiv.)	Time (h)	Convn **1q**, %	Yield **6q**, %
1	H_2O_2 (A, 10)	$BF_3 \cdot Et_2O$ (1)	12	18	trace
2	H_2O_2 (A, 10)	$BF_3 \cdot Et_2O$ (5)	12	86	37
3	**H_2O_2 (A, 10)**	**$BF_3 \cdot Et_2O$ (10)**	**12**	**>95**	**92**
4	H_2O_2 (A, 5)	$BF_3 \cdot Et_2O$ (10)	12	>95	81
5	H_2O_2 (A, 3)	$BF_3 \cdot Et_2O$ (10)	12	>95	67
6	H_2O_2 (A, 2)	$BF_3 \cdot Et_2O$ (10)	12	>95	32
7	H_2O_2 (A, 1)	$BF_3 \cdot Et_2O$ (10)	12	37	trace
8	H_2O_2 (A, 10)	$BF_3 \cdot Et_2O$ (10)	3	>95	83
9	H_2O_2 (A, 10)	$BF_3 \cdot Et_2O$ (10)	1	91	33
10	H_2O_2 (B, 3)	$BF_3 \cdot Et_2O$ (10)	24	91	43
11	H_2O_2 (C, 4)[c]	H_2SO_4 (0.24)	12	41	traces
12	H_2O_2 (C, 4)	H_2SO_4 (10)	12	54	traces
13	H_2O_2 (A, 10)	H_2SO_4 (10)	12	>95	77
14	H_2O_2 (A, 10)	$HClO_4$ (10)	12	92	78
15	H_2O_2 (A, 10)	HBF_4 (10)	12	87	67
16	H_2O_2 (A, 10)	$H_3PMo_{12}O_{40} \cdot xH_2O$ (1)	24	84	66
17	H_2O_2 (A, 10)	$P_2O_5 \cdot 24WO_3 \cdot 44H_2O$ (0.5)	24	90	57
18	H_2O_2 (A, 10)	$Na_2MoO_4 \cdot 2H_2O$ (2)	24	no rxn	-
19	H_2O_2 (A, 10)	I_2 (5)	24	no rxn	-
20	H_2O_2 (A, 10)	I_2 (0.1)	24	no rxn	-
21	H_2O_2 (A, 10)	TBAI (2)	24	>95	**7**, 27[d]

[a] **General procedure**: An ethereal solution of H_2O_2 (2.048 M, 0.488-4.882 mL, 1.0-10.0 mmol, 1-10.0 equiv.) was added with stirring to **1q** (220.3 mg, 1.00 mmol, 1.0 equiv.). The mixture was

cooled to 0°C and acid was added dropwise with stirring. The reaction mixture was then stirred at 20-25 °C for 1, 3, 12 or 24 h. [b] type A – solution of H_2O_2 in Et_2O, molar concentration 2.048 M, type B – urea hydrogen peroxide, type C – 90% H_2O_2. [c] literature procedure[40] [d] 4-phenylbutan-2-one (**7**)

The reaction does not proceed in the presence of an equimolar amount of boron trifluoride, even despite the large excess of hydrogen peroxide (Table 1, entry 1). This observation suggests, that there are unproductive coordination complexes for BF_3 that effectively remove it from the reaction path when only one equivalent of BF_3 is available. On the other hand, raising the excess of $BF_3 \cdot Et_2O$ to 10 equivalents leads to an increase of the target cyclic peroxide yield to 92% (entries 1-3). Entries 4-7 illustrate the key role of the excess of H_2O_2 on the product yield: the yield of 5-hydroperoxy-1,2-dioxolan-3-one **6q** decrease by 60% (entry 6), when 2 equivalents of peroxide were used. When one equivalent of H_2O_2 was used, only traces of desirable peroxide **6q** were observed (entry 7). Using less $BF_3 \cdot Et_2O$ (entry 2) results in the formation of a mixture of the desired peroxide **6q** (37%) and the acyclic geminal bisperoxide (ethyl 2-benzyl-3,3-dihydroperoxybutanoate, 32%). Shorter reaction times (3 hrs and 1 h) lowered the yield by 9% and 59%, respectively (entries 8 and 9).

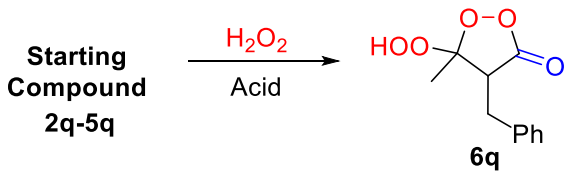
An attempt to use urea/H_2O_2 complex instead of the ethereal solution of hydrogen peroxide showed that use of the latter is essential for reaching the high product yields (entries 5 and 10). Surprisingly, the application of the literature approach to β-hydroperoxy-β-peroxylactones, reported by Cubbon and Hewlett,[40] for synthesis of our target peroxide **6q** did not lead to the formation of β-peroxylactone with 0.24 equiv. of H_2SO_4 (entry 11) or when an even larger amount of the acid was used. Most likely, this result is associated with the instability of the keto group or benzyl moiety under this conditions[73] as well as the difficulties in applying heterogeneous reaction conditions of the Cubbon and Hewlett method to the small amounts of the substrate. Substitution of the dangerous concentrated H_2O_2 to an excess of ethereal H_2O_2 yields target peroxide **6q** in good yields (67-78%, entries 13-15) with use of a 10-fold excess of strong Bronsted acid (H_2SO_4,

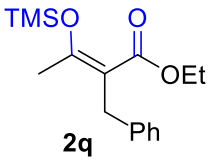
$HClO_4$, HBF_4). Good yields of peroxide **6q** can be also obtained under catalysis by heteropolyacids such as phosphomolybdic (entry 16) and phosphotungstic acids (entry 17) shown earlier to be excellent peroxidation catalysts.[59,74-76] Use of other common peroxidation catalysts such as sodium molybdate[77] (entry 18) and iodine[78] (entries 19, 20) did not promote the reaction. In the case of TBAI,[79] we observed oxidative fragmentation with the formation of 4-phenylbutan-2-one in 27 % (entry 21).

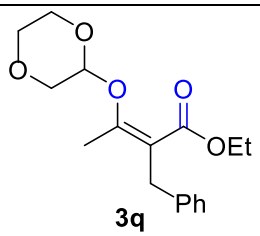
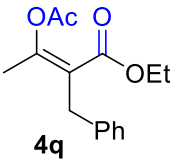
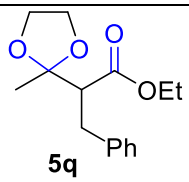
As discussed earlier, the effect of acid equivalents on the formation of β-peroxylactones was large and the cyclization proceeded efficiently only in the presence of a large excess boron trifluoride (10 equivalents). In the acidic media, peroxyesters are known to participate in the Baeyer-Villiger[80-82] and Criegee[83] reactions that involve the O-O bond scission. Under the present conditions, these reactions do not occur.

β-Hydroperoxy-β-peroxylactones can be obtained from enol ethers and acetals despite the presence of alternative oxidation pathways. Synthesis of β-hydroperoxy-β-peroxylactone **6q** was successfully carried out with silyl enol ether **2q**, alkyl enol ether **3q**, enol acetate **4q**, cyclic acetal **5q** instead of β-ketoester **1q** as substrate (Table 2).

Table 2. Synthesis of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one **6q** from silyl enol ether **2q**, alkyl enol ether **3q**, enol acetate **4q**, cyclic acetal **5q** and H_2O_2.



№	Starting Compound	Yield of **6q**, %		
		Substrate/ H_2O_2 (10 equiv.) / $BF_3{\cdot}Et_2O$ (10 equiv.) [a]	**H_2O_2/ $BF_3{\cdot}Et_2O$/ Substrate** other order of addition [b]	**H_2O_2/$HClO_4$/ Substrate** other order of addition and $HClO_4$ instead of $BF_3{\cdot}Et_2O$ [c]
1	 **2q**	61	73	93

2	 **3q**	55	51	86
3	 **4q**	53	39	52
4	 **5q**	92	91	85

[a] **optimal reaction conditions for β-ketoesters**: An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) was added with stirring to starting compound **2q-5q** (1.0 mmol, 1.0 equiv.). Later, $BF_3 \cdot Et_2O$ (10.0 mmol, 10.0 equiv.) was added dropwise with stirring to a solution at 0°C.

[b] **other order of addition of reagents:** $BF_3 \cdot Et_2O$ (10.0 mmol, 10.0 equiv.) was added dropwise with stirring to ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) at 0°C. Later, starting compound **2q-5q** (1.0 mmol, 1.0 equiv.) was added dropwise with stirring to the mixture.

[c] **other order of addition of reagents and with $HClO_4$ instead of $BF_3 \cdot Et_2O$**: $HClO_4$ (10.0 mmol) was added dropwise with stirring to ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) at 0°C. Later, starting compound **2q-5q** (1.0 mmol) was added dropwise with stirring to the mixture.

The reaction mixture was stirred at 20-25 °C for 12 h.

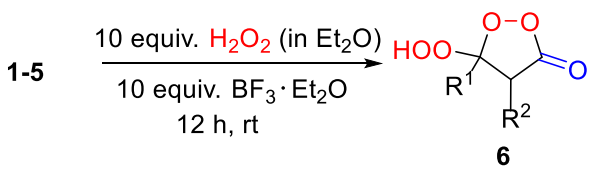
Surprisingly, only peroxide **6q** was formed in the reaction of enol ethers **2q-4q** and acetal **5q** with the H_2O_2/BF_3 system. We have not observed α-oxylated products despite the literature reports that this system acts as peracid in oxidation reactions,[84,85] including the conversion of sulfides to sulfones[86] and aldehydes to carboxylic acids or esters.[87] Furthermore, it is known that reactions of silyl enol ethers from β-ketoesters with MCPBA,[88,89] p-nitrobenzenesulfonyl peroxide[90] and DMDO[91] led to α-hydroxylated products. Enol acetates undergo anodic oxidation in the presence of acetic acid to form conjugated enones, α-acetoxy carbonyl compounds, *gem*-

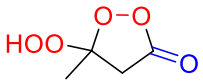
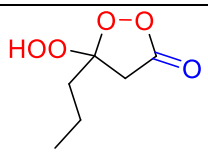
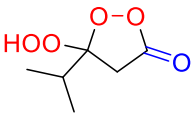
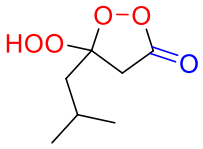
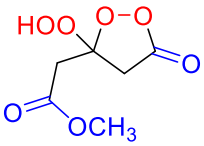
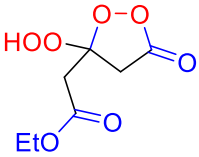
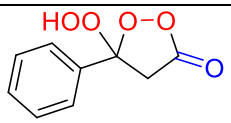
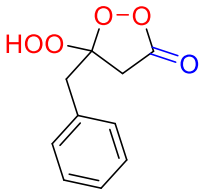
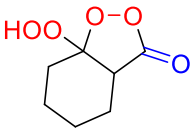
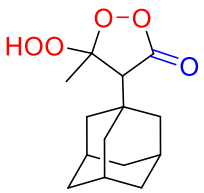
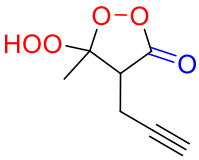
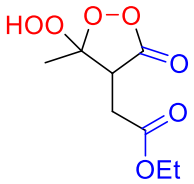
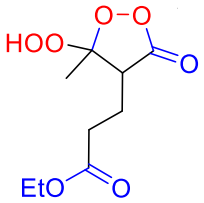
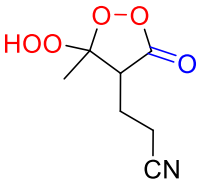
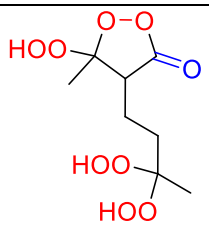
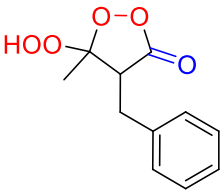
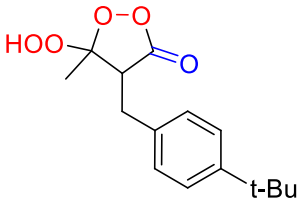
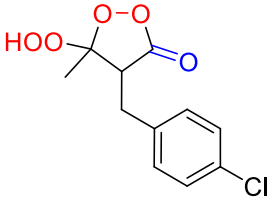
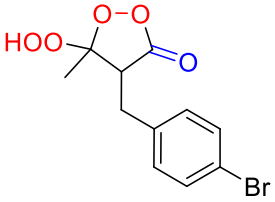
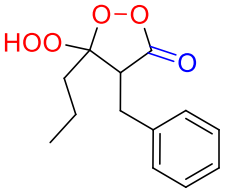
diacetoxy compounds and triacetoxy compounds,[92,93] and in the presence of H_2O_2/NaOH system to α-hydroxylated products.[94] Also α-acetoxy carbonyl compounds can be prepared from enol acetates under action of lead tetraacetate *via* rearrangement of epoxy acetate[95] or under action of peracids.[96]

Under the optimal conditions (Table 1, entry 3), the silyl enol ether **2q** and alkyl enol ether **3q** were transformed into peroxide **6q** in moderate yields 51-73% (Table 2, entries 1 and 2). High yields (93% and 86%) of **6q** were achieved with use of $HClO_4$ instead of $BF_3 \cdot Et_2O$ (Table 2, entries 1 and 2). Peroxidation of enol acetate **4q** (Table 2, entry 3) was achieved only in moderate yields (39-53 %) of **6q** even with the other order of addition of reagents and with $HClO_4$ instead of $BF_3 \cdot Et_2O$ due to the low substrate conversion. With the use of acetal **5q**, high yields (85-92 %) of **6q** were achieved both under the optimal conditions and with the other order of reagent addition (Table 2, entry 4). Surprisingly, the easily oxidizable enol ethers **2q**-**4q** and acetal **5q** do not undergo observable destructive oxidation. Even in the presence of large excesses of a strong oxidant and acid, enol ethers **2q**-**4q** and acetal **5q** are selectively converted to cyclic peroxide **6q**. It is possible that carbonyl coordination with the Lewis acid decreases donor ability of the double bond.

The conditions identified as optimal for synthesis of β-hydroperoxy-β-peroxylactone **6q** from the corresponding β-ketoester (Table 1, entry 3) were utilized for the synthesis of β-hydroperoxy-β-peroxylactones **6a-u** with varying degrees of substitution (Table 3).

Table 3. Scope of β-hydroperoxy-β-peroxylactones **6a-u** synthesized from β-ketoesters **1a-u**[a] and silyl enol ethers **2b, 2e, 2q**, alkyl enol ethers **3a, 3g, 3q**, enol acetates **4g, 4n, 4q**, cyclic acetals **5j, 5o, 5q**.



 **6a**, 88 (from **3a**: 89)[b]	 **6b**, 96 (from **2b**: 88)[c]	 **6c**, 90
 **6d**, 64	 **6e**, 79 (from **2e**: 61)[d]	 **6f**, 78
 **6g**, 61 (from **3g**: 73)[e] (from **4g**: 86)[f]	 **6h**, 77	 **6i**, 87
 **6j**, 57 (from **5j**: 75)[g]	 **6k**, 80	 **6l**, 64
 **6m**, 73	 **6n**, 66 (from **4n**: 30)[h]	 **6o,** 78 (from **5o**: 74)[i]
 **6p**, 56	 **6q**, 92	 **6r**, 76
 **6s**, 93	 **6t**, 81	 **6u**, 90

[a] **General procedure**: An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) was added with stirring to **1a-u** (1.00 mmol, 1.0 equiv.). Later, $BF_3{\cdot}Et_2O$ (1.419 g, 10.00

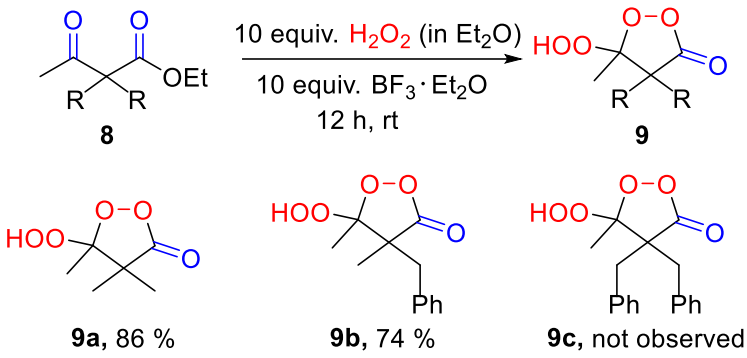
mmol, 10 equiv.) was added dropwise with stirring to the solution at 0 °C. The reaction mixture was stirred at 20-25 °C for 12 h. The values in parentheses – yield of **6** starting from **2-5**.
[b] from ethyl 3-ethoxybut-2-enoate **3a**
[c] from ethyl 3-((trimethylsilyl)oxy)hex-2-enoate **2b**
[d] from dimethyl 3-((trimethylsilyl)oxy)pent-2-enedioate **2e**
[e] from ethyl 3-((1,4-dioxan-2-yl)oxy)-3-phenylacrylate, **3g**
[f] from ethyl 3-acetoxy-3-phenylacrylate, **4g**
[g] from ethyl 1,4-dioxaspiro[4.5]decane-6-carboxylate **5j**
[h] from diethyl 2-(1-acetoxyethylidene)pentanedioate **4n**
[i] from ethyl 4-cyano-2-(2-methyl-1,3-dioxolan-2-yl)butanoate **5o**

The α-unsubstituted β-hydroperoxy-β-peroxylactones **6a-h** were obtained from β-ketoesters **1a-h** in good (61% for **6g**) to excellent yields (96% for **6b**). Fusion of the β-peroxylactone ring to a cycloalkane provided bicyclic peroxides **6i**, **6j** in 87% and 57%, respectively. The preparation of β-hydroperoxy-β-peroxylactones with bulky adamantyl (**6k**, 80%), propargyl (**6l**, 64%), ester (**6m**, 73%; **6n**, 66%) and nitrile (**6o,** 78%) functionalities, as well as the tetraperoxide that combined a β-hydroperoxy-β-peroxylactone and a *gem*-dihydroxyperoxide moieties (**6p**, 56%) proceeded in good yields. Presence of benzylic group increases the yields of β-hydroperoxy-β-peroxylactones - products **6q-u** were obtained in 76-93% yields. The flexibility of this approach in selection of starting materials is illustrated by facile formation of β-hydroperoxy-β-peroxylactones from enols **2-4** and acetals **5**, as well as the *t*-Bu esters of β-ketoesters (compound **6t**). β-Hydroperoxy-β-peroxylactones **6b** and **6e** were prepared from silyl enol ethers **2b** and **2e** (notes c and d) in good (61% for **6e**) and high (88% for **6b**) yields. Use of the enol ethers **3a** and **3g** (notes b and e) instead of β-ketoesters **1a** and **1g** increased the yields of **6a** (89%) and **6g** (73%). Synthesis of β-hydroperoxy-β-peroxylactone **6g** from enol acetate **4g** (note f) led to the highest observed yield of **6g** (86%). However, synthesis of **6n** from enol acetate **4n** (note h) was less efficient (30%) than from β-ketoester **1n** (66%). Peroxidation of acetals **5j** and **5o** (notes g and i) provided good yield of the desirable β-hydroperoxy-β-peroxylactones **6j** (75%) and **6o** (74%).

The oxidative properties of the synthesized β-hydroperoxy-β-peroxylactones were investigated with cyclic voltammetry. It was shown that reduction potentials for the β-

peroxylactones **6d** and **6q** (-1091 mV and -1026 mV, respectively) are lower than the potentials for bridged 1,2,4,5-tetraoxane (1,4-dimethyl-7-(1-(p-tolyl)ethyl)-2,3,5,6-tetraoxabicyclo[2.2.1] heptane, -1319 mV) but greater than the potentials for cyclopropyl malonyl peroxide (-603 mV). These findings illustrate moderate oxidative properties of β-hydroperoxy-β-peroxylactones (Scheme S1, Supplementary Information).

The nature of the second substrate at the α-position of β-ketoesters **8** greatly affects the peroxidation process. Thus, α,α-dimethyl β-ketoester **8a** formed desired β-hydroperoxy-β-peroxylactone **9a** with excellent (86%) yield in optimized condition (Table 1, entry 3), while α-methyl, α-benzyl β-ketoester **8b** was transformed into peroxide **9b** in a slightly lower yield (74%) and peroxidation of α,α-dibenzyl β-ketoester **8c** did not lead to formation of **9c** (Scheme 5).



Scheme 5. Peroxidation of α,α-disubstituted β-ketoesters **8**.

The unambiguous NMR determination of structure of organic peroxides can be challenging because of the possibility of condensation of several molecular units *via* the peroxide bridges and because of the possibility of acid-catalyzed skeletal rearrangements. To address this difficulty, we have performed X-ray crystallographic analysis of several representatives (**6q** and **6s**, Supplementary Information) of this scarcely studied class of β-peroxylactones (Figure 1). In addition to confirming the presence of two peroxide units, the X-ray data unambiguously determined the nature of the diastereomeric product (formed as a single isomer according to ^{1}H and ^{13}C NMR spectra) for β-hydroperoxy-β- peroxylactones **6q** and **6s**.

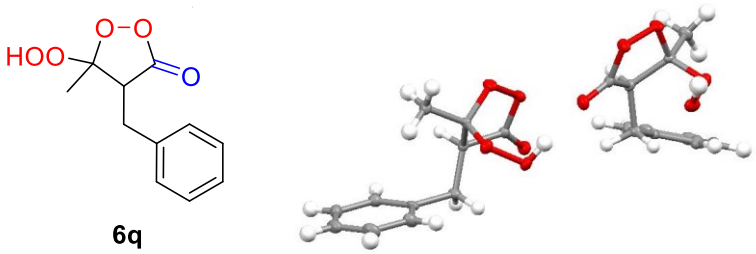
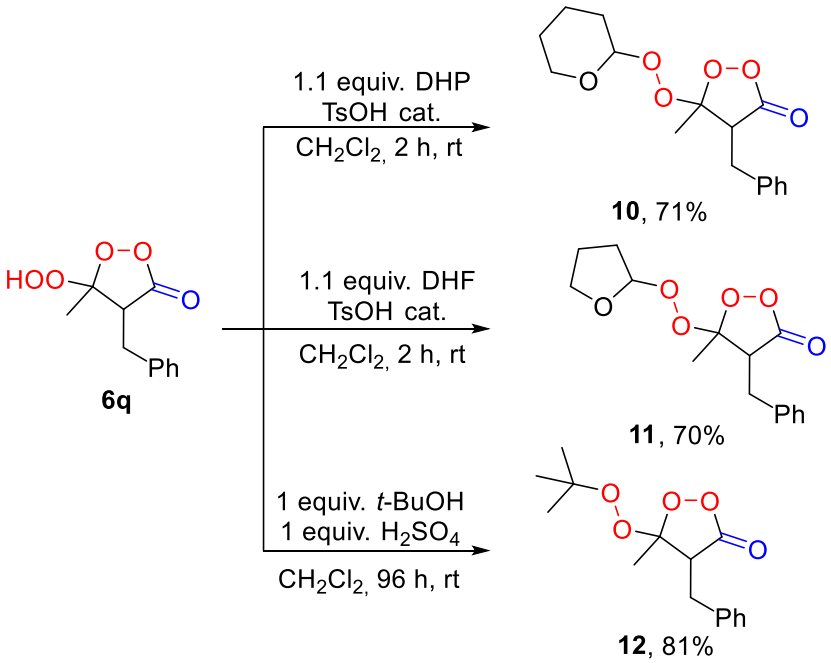


Figure 1. X-ray structure of β-hydroperoxy-β-peroxylactone **6q**.

In order to gain first insights into the chemistry of this scarcely studied class of peroxides, we have investigated further synthetic transformations of β-hydroperoxy-β-peroxylactones. As expected from the synthetic conditions used for their preparation, the β-hydroperoxy-β-peroxylactone functionality is stable under the acidic conditions. We found that the hydroperoxide functionality in **6q** can be protected *via* installation of tetrahydropyranyl (THP), tetrahydrofuranyl (THF) and *t*-Bu groups (Scheme 6).

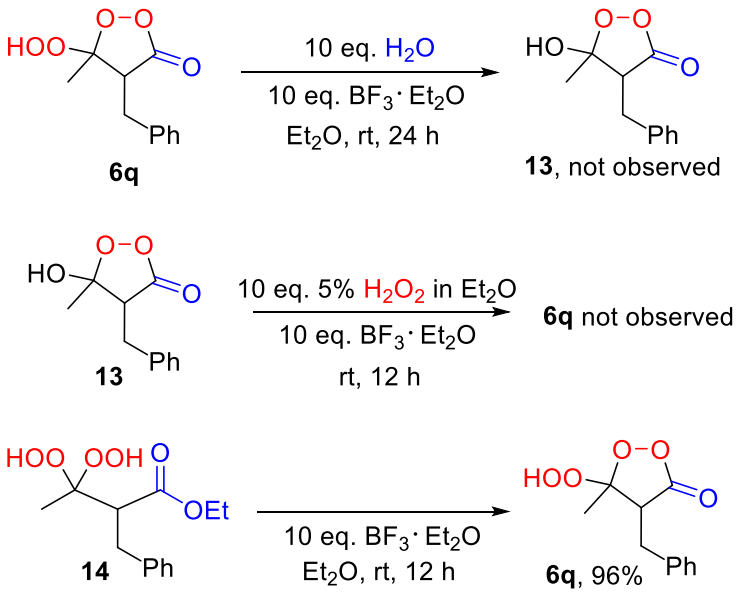


Scheme 6. Transformations of hydroperoxy group in β-hydroperoxy-β-peroxylactone **6q**.

Mechanistic studies:

Control experiments designed to provide an insight in the mechanism of the product formation (Scheme 7), revealed that β-hydroperoxy-β-peroxylactone **6q** does not equilibrate with β-hydroxy-β-peroxylactone **13** under these conditions. On the other hand, acyclic bishydroperoxide **14** is converted into the β-hydroperoxy-β-peroxylactone **6q** readily and in an almost quantitative yield. The low reactivity of these mono- and bisperoxides under the acidic conditions is likely to originate from the "inverse intramolecular α-effect" (the relatively inefficient stabilization of cationic center by an adjacent peroxide in comparison to ethers, further exacerbated here by the presence of a carbonyl substituent at the peroxide).[97,98]

Because of this effect, peroxides are more reluctant to be converted into cationic intermediates and may possess greater kinetic stability than the analogous ethers and alcohols that are readily transformed into oxacarbenium ions.

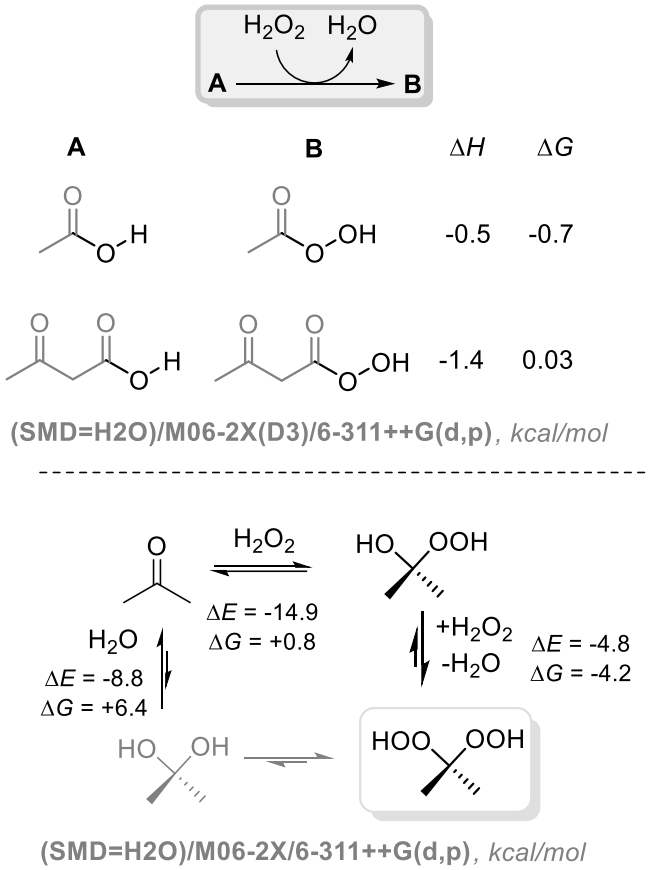


Scheme 7. Experimental evaluation of stability of β-peroxylactones.

Computational analysis of reaction pathways

In order to understand the relative stabilities of the possible intermediates involved in the formation of the new bisperoxides,[63,99] we decided to chart the energy landscape for the interaction of carbonyl compounds and H_2O_2 by using quantum-mechanical calculations.

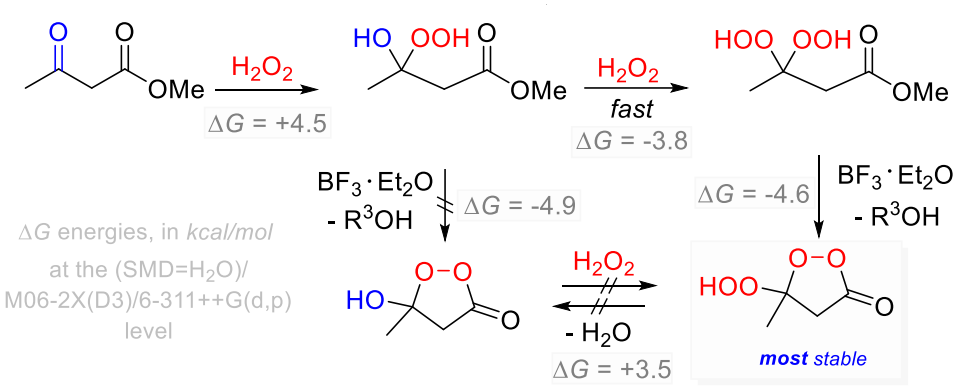
As the first step, we have evaluated thermodynamics for the interaction of key hydroxyl containing functionalities with hydrogen peroxide. Interestingly, the transformation of carboxylic acids into peroxyacids in reaction with H_2O_2 is either weakly exergonic or thermoneutral. For the ketones the situation is slightly different (Scheme 8). The addition of the first H_2O_2 molecule to acetone is slightly endergonic and the resulting unstable mixed monoperoxide are unlikely to be persistent under the reaction conditions. On the other hand, the transformations of acetone and its hydrate into respective bishydroperoxy ketal are sufficiently exergonic to assure the preferential formation of such bishydroperoxides at the equilibrium in the presence of sufficient amounts of hydrogen peroxide.



Scheme 8. Calculated thermodynamic parameters for the interaction of H_2O_2 with selected carboxylic acids and acetone.

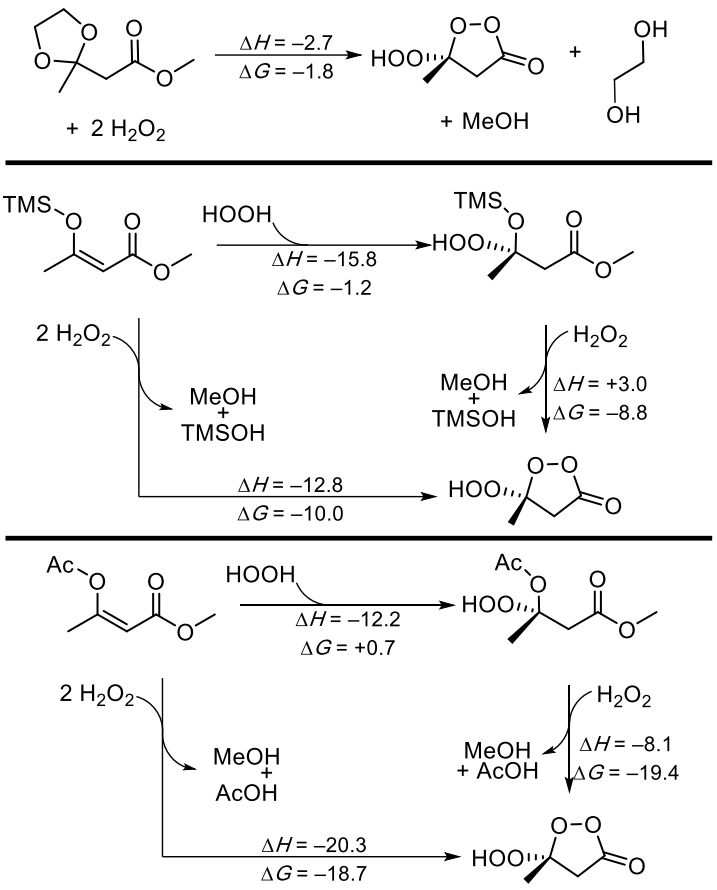
In the next stage, we have explored energy profiles for the interaction of β-ketoacids and esters with hydrogen peroxide. From the two alternative pathways to the target cyclic structure, we

favor the one that start from peroxidation of the carbonyl functions. Furthermore, based on the experimental observations reported in Scheme 7 and reiterated in Scheme 9 below, we suggest the ketoester is transformed into a bishydroperoxide first and that it is the latter species that undergoes the cyclization to form the β-peroxylactone. The cyclization of the mixed hydroxy/hydroperoxy ketal can be discarded based on the observation that β-hydroxy-β-peroxylactone is not transformed into β-hydroperoxy-β-peroxylactone under the reaction conditions. Apparently, the bisperoxide is formed and cyclized quickly to provide the cyclic bisperoxide, the most stable species at this reaction hypersurface.



Scheme 9. Suggested mechanism for synthesis of β-hydroperoxy-β-peroxylactones with the calculated free energies for the formation of the intermediate structures.

We have also evaluated thermodynamics for the formation of the cyclic β-hydroperoxy-β-peroxylactones from cyclic acetals, enol acetates and silyl enol ethers. Gratifying, all of these transformations are exergonic, suggesting that the β-peroxylactones are indeed an energy minimum that connects a variety of the interconverting oxygen-rich species at this combined potential energy surface (Scheme 10). Especially noteworthy is the fact that β-peroxylactones can be formed exergonically from cyclic acetal, a functional group that is strongly stabilized by anomeric effect.[100] This observation provides another illustration of the increased thermodynamic stability of bisperoxides where the anomeric effects (generally dormant in mono-peroxides) are reactivated.[34,35,97,101]



Scheme 10. Thermodynamical landscape for synthesis of β-hydroperoxy-β-peroxylactones from cyclic acetals, enol acetates, and silyl enol ethers derived from β-ketoesters.

CONCLUSION

β-Hydroperoxy-β-peroxylactones can be prepared in moderate to excellent yields from five different types of substrates: β-ketoesters and their silyl enol ethers, alkyl enol ethers, enol acetates, and cyclic acetals. A broad scope of β-hydroperoxy-β-peroxylactones, both α-unsubstituted and α-mono- and α,α-disubstituted, was synthesized. A large excess of $BF_3 \cdot Et_2O$ and H_2O_2 is a key factor determining the selectivity and efficiency of formation of β-hydroperoxy-β-peroxylactones that allows to prepare the target cyclic peroxides in >90% yields.

The computationally evaluated thermodynamics for the formation of the β-hydroperoxy-β-peroxylactones from β-ketoesters, silyl enol ethers, enol acetates, and cyclic acetals confirm that the β-peroxylactone species correspond to an energy minimum that connects a variety of species at

this combined potential energy surface. Furthermore, the β-hydroperoxy-β-peroxylactones are stable in acidic conditions and can be modified *via* hydroperoxyl group functionalization.

EXPERIMENTAL SECTION

Caution: Although we have encountered no difficulties in working with peroxides, precautions such as the performance of reactions within a fume hood and behind a safety shield should be taken. The use of redox-active transition-metal salts, heating and vigorous shaking should be avoided!

NMR spectra were recorded on commercial instrument (300.13 MHz for ^{1}H, 75.48 MHz for ^{13}C) in $CDCl_3$. High resolution mass spectra (HRMS) were measured using electrospray ionization (ESI-TOF).[102] The measurements were done in a positive ion mode (interface capillary voltage – 4500 V); mass range from m/z 50 to m/z 3000 Da; external/internal calibration was done with Electrospray Calibrant Solution. A syringe injection was used for solutions in MeCN (flow rate 3 μL/min). Nitrogen was applied as a dry gas; interface temperature was set at 180 °C.

The TLC analysis was carried out on standard silica gel chromatography plates. The melting points were determined on a Kofler hot-stage apparatus. Chromatography was performed on silica gel (40-60 μm).

Ethyl acetoacetate (**1a**), ethyl butyrylacetate (**1b**), dimethyl 1,3-acetonedicarboxylate (**1e**), ethyl benzoylacetate (**1g,** was distilled before use under reduced pressure (15-20 mmHg)), ethyl 2-oxocyclopentanecarboxylate (**1i**), ethyl 2-oxocyclohexanecarboxylate (**1j**), diethyl acetylsuccinate (**1m**), H_2O_2 (37% solution in water), $BF_3{\cdot}Et_2O$, I_2, p-TsOH monohydrate, H_2SO_4, $HClO_4$ (70% solution in water), HBF_4 (48% solution in water), $NaHCO_3$, phosphomolybdic acid hydrate (formula weight: 1,825.25 g/mol), phosphotungstic acid hydrate (formula weight: 2,880.05 g/mol), $Na_2MoO_4{\cdot}2H_2O$, tetrabutylammonium iodide, urea hydrogen peroxide, 3,4-dihydro-2H-pyran, 2,3-dihydrofuran, *t*-BuOH, Bu_4NClO_4, Et_3N, TMSCl, K_2CO_3, Na, NaH (60% in mineral oil), NaOH, TEBAC, triethyl orthoformate, $Cu(OAc)_2{\cdot}H_2O$, 1,4-dioxane, 5-6 M TBHP solution in

decane, pyridine, acetyl chloride, $CuSO_4 \cdot 5H_2O$, ethylene glycol, methyl iodide were purchased from commercial sources and were used as is. All solvents were distilled before use using standard procedures.

Distillation of the commercial ethyl benzoylacetate **1g** was performed under medium vacuum (10 mmHg). Fraction with bp = 129-134 °C was collected and used in peroxide synthesis.

A solution of H_2O_2 in Et_2O (2.048 mol/L, ≈9.8% weight) was prepared by the extraction with Et_2O (5 × 100 mL) from a 35% aqueous solution (100 mL) followed by drying over $MgSO_4$.[64,103] Solution of H_2O_2 in Et_2O (90 % weight) prepared by evaporated of 9.8% solution of H_2O_2 in Et_2O.

Synthesis of starting β-ketoesters 1

Procedure for the synthesis of ethyl 4-methyl-3-oxopentanoate (1c) [104]

Isobutyric acid (2.91 g, 33.0 mmol, 1.0 equiv.) was dissolved in dry CH_2Cl_2 (140 mL). Meldrum's acid (5.23 g, 36.3 mmol, 1.1 equiv.) and 4-(dimethylamino)-pyridine (6.11 g, 50.0 mmol, 1.5 equiv.) were added and the mixture was stirred at 20-25 °C for 15 min. After cooling to 0 °C, a solution of dicyclohexylcarbodiimide (8.26 g, 40.0 mmol, 1.2 equiv.) in dry CH_2Cl_2 (10 mL) was added and the reaction mixture stirred at 20-25 °C for 10 h. The precipitate containing dicyclohexylurea was filtered off and the filtrate was washed with a 10% aqueous solution of citric acid (2×20 mL), brine (20 mL) and dried over $MgSO_4$. The organic phase was concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C) and was applied to the next reaction step without purification. The crude 5-(1-hydroxy-2-methylpropylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione was refluxed in toluene (80mL) with EtOH (20 mL) for 3 h. Then reaction mixture was concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 80–85 °C). The product **1c** was isolated by column chromatography on SiO_2 (PE:EtOAc = 10:1). Yield 43 % (2.24 g, 14.2 mmol). Yellow oil. R_f = 0.67 (PE:EtOAc = 20:1). Keto/enol ratio = 9/1. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 12.12 (s, 0.1H), 4.96 (s, 0.1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.47 (s, 1.8H), 2.70 (sept, *J* = 6.9 Hz, 0.9H),

2.45 – 2.31 (m, 0.1H), 1.25 (t, J = 7.1 Hz, 3H), 1.11 (d, J = 6.9 Hz, 6H). $^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 206.7, 167.5, 86.8, 61.4, 60.0, 47.2, 41.3, 19.8, 18.0, 14.2. The physical and spectral data were consistent with those previously reported.[104]

Procedure for the synthesis of ethyl 5-methyl-3-oxohexanoate (1d) [105]

NaH (60% in mineral oil, 1.20 g, 30.0 mmol, 1.5 equiv.) was added to dry toluene (20 mL). The diethyl carbonate (3.54 g, 30.0 mmol, 1.5 equiv.) was added to the stirred suspension. Then a solution of 4-methylpentanone-2 (2.00 g, 20.0 mmol, 1.0 equiv.) in dry toluene (20 mL) was added dropwise. In the middle of the process of addition one drop of absolute EtOH was added. The reaction mixture was refluxed with stirring for 3 h. After cooling to 20–25 °C the reaction was acidified to pH ~6 by careful addition of 5% aq. HCl (50 mL). Organic layer was separated, aqua layer was extracted with Et_2O (3×20 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure (15-20 mmHg), (bath temperature, ca. 40–45 °C). The product **1d** was isolated by column chromatography on SiO_2 (PE:EtOAc = 15:1). Yield 47 % (1.62 g, 9.4 mmol). Yellow oil. R_f = 0.21 (PE:EtOAc = 20:1). Keto/enol ratio = 9/1. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 12.06 (s, 0.1H), 4.93 (s, 0.1H), 4.18 (q, J = 7.1 Hz, 2H), 3.39 (s, 1.8H), 2.40 (d, J = 6.9 Hz, 2H), 2.24 – 2.05 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H), 0.92 (d, J = 6.6 Hz, 6H). $^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 202.6, 167.3, 90.1, 61.4, 52.0, 49.8, 44.5, 24.4, 22.5, 22.5, 14.2. The physical and spectral data were consistent with those previously reported.[105]

Procedure for the synthesis of diethyl 1,3-acetonedicarboxylate (1f) [106]

Citric acid monohydrate (2.10 g, 10.0 mmol, 1.0 equiv.) was added to chlorosulfonic acid (2.5 mL, 38 mmol, 3.8 equiv.) in CH_2Cl_2 (3 mL) at 10 °C. After 5 h the reaction mixture was cooled (0-5 °C) and EtOH (5 mL) added carefully to ensure the temperature did not exceed 35 °C. After stirring for 2 h at 35-40 °C, the reaction was cooled, H_2O (10 mL) was added, and reaction was extracted with CH_2Cl_2 (3×20 mL). The organic phase was washed with 5 % solution of $NaHCO_3$

(10 mL) and H_2O (10 mL), dried over $MgSO_4$ and concentrated under reduced pressure (15-20 mmHg), (bath temperature, ca. 30–35 °C). The product **1f** was isolated by column chromatography on SiO_2 (PE:EtOAc = from 20:1 to 2:1). Yield 53 % (1.07 g, 5.3 mmol). Yellow oil. R_f = 0.76 (PE:EtOAc = 20:1). Keto/enol ratio = 5/1. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 12.08 (s, 0.17H), 5.11 (s, 0.17H), 4.18 (q, *J* = 7.1 Hz, 4H), 3.59 (s, 3.3H), 3.20 (s, 0.35H), 1.26 (t, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 195.5, 172.4, 170.0, 166.8, 92.1, 61.7, 61.5, 60.4, 49.1, 41.1, 14.3, 14.2, 14.1. The physical and spectral data were consistent with those previously reported.[106]

Procedure for the synthesis of ethyl 3-oxo-4-phenylbutanoate (1h)[107]

Substrate **1h** was synthesized according to the modified literature procedure.[4] To a suspension of phenylacetic acid (816.0 mg, 6.0 mmol, 1.0 equiv.) in dry CH_2Cl_2 (10 mL), CDI (1.05 g, 6.5 mmol, 1.08 equiv.) was added. After stirring for 0.5 h, Meldrum's acid (1.081 g, 7.5 mmol, 1.25 equiv.) was added and stirred for additional 12 h. Then the reaction mixture was poured into 5% HCl (30 mL) and extracted with CH_2Cl_2 (3×10 mL). The extract was washed with 5% HCl (25 mL) and with H_2O (25 mL) and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 30–35 °C). To the residue, EtOH (10 mL) was added and the resulting mixture was refluxed for 2 h. The obtained solution was concentrated and 5% $NaHCO_3$ (30 mL) was added to the residue. The obtained mixture was extracted with ethyl acetate (3×10 mL). The extract was washed with H_2O (10 mL), filtered through thin layer of silica gel (2 cm) and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 30–35 °C). The product **1h** was isolated by column chromatography on SiO_2 (PE:EtOAc = from 20:1 to 2:1). Yield 66 % (817.0 mg, 4.0 mmol). Yellow oil. R_f = 0.67 (PE:EtOAc = 20:1). Keto form: ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.42 – 7.13 (m, 5H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 2H), 3.43 (s, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 200.5, 167.2, 133.3, 129.7, 128.9, 127.4, 61.5, 50.1, 48.4, 14.2. The physical and spectral data were consistent with those previously reported.[107]

Procedure for the synthesis of ethyl 2-(adamantan-1-yl)-3-oxobutanoate (1k) [108]

$Cu(OTf)_2$ (90.4 mg, 0.25 mmol, 0.05 equiv.) was added to dry 1,2-dichloroethane (5 mL). Then a solution of 1-adamantanol (761.2 mg, 5.00 mmol, 1 equiv.) and ethyl acetoacetate (650.7 mg, 5.00 mmol, 1 equiv.) in dry 1,2-dichloroethane (10 mL) was added. The reaction mixture was refluxed with stirring for 2 h. After cooling to 20–25 °C, 2 M HCl (10 mL) was added. The organic layer was separated and the product was extracted from the aqueous phase with $CHCl_3$ (3×10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 30–35 °C). The product **1k** was isolated by column chromatography on SiO_2 (PE:EtOAc = 20:1). Yield 74 % (978.2 mg, 3.7 mmol). Yellow oil. R_f = 0.57 (PE:EtOAc = 20:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.15 (q, *J* = 7.1 Hz, 2H), 3.17 (s, 1H), 2.21 (s, 3H), 2.00 – 1.94 (m, 3H), 1.80 – 1.62 (m, 13H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 203.3, 168.8, 70.1, 60.8, 40.2, 37.1, 36.8, 32.1, 28.8, 14.3. The physical and spectral data were consistent with those previously reported.[108]

Ethyl 2-acetylpent-4-ynoate (1l)

Product **1l** was synthesized according to the literature procedure.[109] Yield 67 % (2.53 g, 15.0 mmol) Yellow oil. R_f = 0.63 (PE:EtOAc = 10:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.22 (q, *J* = 7.1 Hz, 2H), 3.68 (t, *J* = 7.0 Hz, 1H), 2.70 (d, *J* = 7.0 Hz, 2H), 2.29 (s, 3H), 1.98 (t, *J* = 2.6 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 201.2, 168.2, 80.5, 70.4, 62.0, 58.4, 29.7, 17.5, 14.2. The physical and spectral data were consistent with those previously reported.[109]

Procedure for the synthesis of diethyl 2-acetylpentanedioate (1n)

Na (0.69 g, 0.03 mol, 0.2 equiv.) was added to dry EtOH (5 mL). Resulting solution of EtONa was cooled to room temperature and added to mixture ethyl acetoacetate (29.25 g, 0.225 mol, 1.5 equiv.) and ethyl acrylate (15.02 g, 0.15 mol, 1.0 equiv.) with stirring. The reaction mixture was stirred over night at 20-25 °C. Then CH_2Cl_2 (100 mL) was added, mixture was washed with 5%

solution of $NaHCO_3$ (2×50 mL), brine (50 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). Distillation of the remaining liquid under medium vacuum (8.00 mmHg) gave product **1n** as third fraction (bp = 165-175 °C). Yield 55 % (19.10 g, 83.0 mmol). Colorless oil. R_f = 0.65 (PE:EtOAc = 20:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.18 (q, *J* = 7.2 Hz, 2H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.53 (t, *J* = 7.2 Hz, 1H), 2.36 – 2.29 (m, 2H), 2.23 (s, 3H), 2.17 – 2.08 (m, 2H), 1.29 – 1.20 (m, 6H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 202.6, 172.7, 169.4, 61.6, 60.6, 58.5, 31.6, 29.2, 23.1, 14.3, 14.2. The physical and spectral data were consistent with those previously reported.[110]

Procedure for the synthesis of ethyl 2-acetyl-4-cyanobutanoate (1o)

Na (69.0 mg, 3.00 mmol, 2.0 equiv.) was added to dry EtOH (1 mL). Resulting solution of EtONa was cooled to room temperature and added to mixture ethyl acetoacetate (292.8 mg, 2.25 mmol, 1.5 equiv.) and acrylonitrile (79.6 mg, 1.50 mmol, 1.0 equiv.) with stirring. The reaction mixture was stirred over night at 20-25 °C. Then CH_2Cl_2 (10 mL) was added, mixture was washed with 5% solution of $NaHCO_3$ (2×3 mL), brine (3 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). The product **1o** was isolated by column chromatography on SiO_2 (PE:EtOAc = 10:1). Yield 80 % (220.0 mg, 1.20 mmol). Yellow oil. R_f = 0.58 (PE:EtOAc = 10:1). Keto/enol ratio = 4/1. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 12.87 (s, 0.2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.63 (t, *J* = 7.1 Hz, 0.8H), 2.43 (t, *J* = 7.1 Hz, 2H), 2.28 (s, 3H), 2.20 – 2.08 (m, 2H), 1.28 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 201.4, 168.4, 118.7, 62.1, 57.4, 29.6, 23.4, 15.2, 14.1. The physical and spectral data were consistent with those previously reported.[111]

Procedure for the synthesis of ethyl 2-acetyl-5-oxohexanoate (1p)

$CeCl_3 \cdot 7H_2O$ (111.8 mg, 0.30 mmol, 0.1 equiv.) was heated at 150 °C for 2 h, after cooling to room temperature cerium chloride was added with vigorous stirring to ethyl acetoacetate (390.0 mg, 3.00 mmol, 1.0 equiv.). The mixture was stirred at room temperature for 5 min, and then

methyl vinyl ketone (231.3 mg, 3.30 mmol, 1.1 equiv.) and NaI (22.5 mg, 0.15 mmol, 0.05 equiv.) were added. The reaction mixture was stirred at room temperature for 24 h and filtered. The precipitate was washed with a PE:EtOAc mixture (1:2, v/v). The solvent was evaporated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). The product **1p** was isolated by column chromatography on SiO_2 (PE:EtOAc = 2:1). Yield 73 % (438.3 mg, 2.19 mmol). Colorless oil. R_f = 0.30 (PE:EtOAc = 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.17 (q, *J* = 7.2 Hz, 2H), 3.47 (t, *J* = 7.2 Hz, 1H), 2.48 (t, *J* = 7.1 Hz, 2H), 2.22 (s, 3H), 2.11 (s, 3H), 2.09 – 2.00 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 207.6, 202.9, 169.6, 61.6, 58.4, 40.6, 30.0, 29.1, 21.8, 14.2. The physical and spectral data were consistent with those previously reported.[34]

General procedure for the synthesis of β-ketoesters 1q-s (GP1).

Ethyl acetoacetate (19.5 g, 0.15 mol, 1.0 equiv.) was added with vigorous stirring to the mixture of powdery NaOH (6.0 g, 0.15 mol, 1.0 equiv.) and TEBAC (171.0 mg, 0.75 mmol, 0.005 equiv.) in dry benzene (10 mL). After 15 minutes corresponding benzyl bromide (30.8-40.9 g, 0.18 mol, 1.2 equiv.) was added with stirring dropwise at 50-60 °C. The reaction mixture was stirred at the same temperature for 3 h. Later, the residue was filtered and washed by Et_2O (3×20 mL). Combined organic fractions were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). Distillation of the remaining liquid under medium vacuum (10 mmHg) gave products **1q-s**.

Ethyl 2-benzyl-3-oxobutanoate (**1q**) [112]

According to **GP1** ethyl acetoacetate (19.5 g, 0.15 mol, 1.0 equiv.) was treated with NaOH (6.0 g, 0.15 mol, 1.0 equiv.) and benzyl bromide (30.8 g, 0.18 mol, 1.2 equiv.) to afford ethyl 2-benzyl-3-oxobutanoate **1q** (25.7 g, 0.12 mol, 78 %) as a colorless oil. bp = 167-168 °C (10 mmHg). R_f = 0.76 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.31 – 7.14 (m, 5H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.77 (t, *J* = 7.6 Hz, 1H), 3.16 (d, *J* = 7.6 Hz, 2H), 2.18 (s, 3H), 1.20 (t, *J* = 7.2 Hz, 3H).

$^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 202.6, 169.2, 138.3, 128.9, 128.7, 126.8, 61.6, 61.4, 34.1, 29.7, 14.1. The physical and spectral data were consistent with those previously reported.[50]

Ethyl 2-(4-(*tert*-butyl)benzyl)-3-oxobutanoate (1r) [113]

According to **GP1** ethyl acetoacetate (19.5 g, 0.15 mol, 1.0 equiv.) was treated with NaOH (6.0 g, 0.15 mol, 1.0 equiv.) and 4-*tert*-butylbenzyl bromide (40.9 g, 0.18 mol, 1.2 equiv.) to afford ethyl 2-(4-(*tert*-butyl)benzyl)-3-oxobutanoate (29.85 g, 0.11 mol, 72 %) as a yellow oil. bp = 183-185 °C (10 mmHg). R_f = 0.81 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.29 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.77 (t, *J* = 7.6 Hz, 1H), 3.13 (d, *J* = 7.6 Hz, 2H), 2.19 (s, 3H), 1.29 (s, 9H), 1.20 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 202.7, 169.4, 149.6, 135.2, 128.6, 125.6, 61.6, 61.5, 34.5, 33.6, 31.5, 29.7, 14.1. The physical and spectral data were consistent with those previously reported.[50]

Ethyl 2-(4-chlorobenzyl)-3-oxobutanoate (1s)

According to **GP1** ethyl acetoacetate (19.5 g, 0.15 mol, 1.0 equiv.) was treated with NaOH (6.0 g, 0.15 mol, 1.0 equiv.) and 4-chlorobenzyl bromide (37.0 g, 0.18 mol, 1.2 equiv.) to afford ethyl 2-(4-chlorobenzyl)-3-oxobutanoate (22.5 g, 0.09 mol, 59 %) as a yellow oil. bp = 108-110 °C (0.1 mmHg). R_f = 0.81 (PE:EtOAc = 5:1). Keto/enol ratio = 9/1. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 12.94 (s, 0.1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.72 (t, *J* = 7.6 Hz, 0.9H), 3.52 (s, 0.2H), 3.17 – 3.08 (m, 1.8H), 2.19 (s, 2.7H), 2.03 (s, 0.3H), 1.20 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 202.1, 169.0, 136.8, 132.6, 130.3, 128.8, 61.7, 61.3, 33.3, 29.7, 14.1. The physical and spectral data were consistent with those previously reported.[114]

Procedure for the synthesis of *tert*-butyl 2-(4-bromobenzyl)-3-oxobutanoate (1t) [115]

60% Suspension in mineral oil NaH (160.0 mg, 4.0 mmol, 1.0 equiv.) was added with stirring to dry THF (5 mL) at 0 °C. Later *tert*-butyl acetoacetate (1.27 g, 8.0 mmol, 2.0 equiv.) and 4-bromobenzyl bromide (1.0 g, 4.0 mmol, 1.0 equiv.) were added with stirring at 0 °C. The reaction mixture was heated to 50 °C and stirred for 2 days. Then mixture was concentrated under reduced

pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). H_2O (10 mL) was added, aqueous layer was washed CH_2Cl_2 (3×20 mL). Combined organic layers were washed with 5% solution of $NaHCO_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). The product **1t** was isolated by column chromatography on SiO_2 (PE:EtOAc = 10:1). Yield 60 % (772.2 mg, 2.4 mmol). Colorless oil. R_f = 0.46 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.38 (d, *J* = 8.2 Hz, 2H), 7.05 (d, *J* = 8.2 Hz, 2H), 3.63 (t, *J* = 7.6 Hz, 1H), 3.11 – 3.01 (m, 2H), 2.19 (s, 3H), 1.39 (s, 9H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 202.4, 168.1, 137.6, 131.7, 130.8, 120.6, 82.5, 62.2, 33.3, 29.6, 28.0. The physical and spectral data were consistent with those previously reported.[115]

Procedure for the synthesis of ethyl 2-benzyl-3-oxohexanoate (1u).[116]

The ethyl 3-oxohexanoate (1.03 g, 6.50 mmol, 1.3 equiv.) was added dropwise to a suspension of K_2CO_3 (5.52 g, 40.0 mmol, 8 equiv.) in dry acetone (10 mL). Then benzyl bromide (857.0 mg, 5.0 mmol, 1 equiv.), KI (41.5 mg, 0.25 mmol, 0.05 equiv.) and dibenzo-18-crown-6 (90.0 mg, 0.25 mmol, 0.05 equiv.) were added. The reaction mixture was refluxed for 10 h. Then aqueous solution of 2M HCl (25 mL) was added and the product from the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). The β-ketoester **1u** was isolated by column chromatography on SiO_2 (PE:EtOAc = from 20:1 to 2:1). Yield 71 % (882.0 mg, 3.6 mmol). Colorless oil. R_f = 0.68 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.31 – 7.11 (m, 5H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.77 (t, *J* = 7.6 Hz, 1H), 3.15 (d, *J* = 7.6 Hz, 2H), 2.51 (dt, *J* = 17.3, 7.2 Hz, 1H), 2.31 (dt, *J* = 17.3, 7.2 Hz, 1H), 1.60 – 1.45 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 204.8, 169.2, 138.4, 128.9, 128.6, 126.7, 61.5, 60.7, 44.8, 34.2, 16.9, 14.1, 13.6. The physical and spectral data were consistent with those previously reported.[117]

Synthesis of enol ethers 2-4 and acetals 5

General Procedure for the synthesis of silyl enol ethers 2. [118]

Et_3N (1.53 g, 15.0 mmol, 1.5 equiv.) was added to a solution of β-ketoester **1** (1.58-2.20 g, 10.0 mmol, 1.0 equiv.) in dry benzene (20 mL) with stirring at 20 °C. Then trimethyl chlorosilane (1.62 g, 15.0 mmol, 1.5 equiv.) was added. The reaction mixture was stirred over night at 20-25 °C. The precipitate was filtered, filtrate was concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C).

Ethyl 3-((trimethylsilyl)oxy)hex-2-enoate, 2b

Yield 87 % (2.00 g, 8.7 mmol). Colorless oil. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 5.10 (s, 0.25H), 5.06 (s, 0.75H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.71 – 2.63 (m, 1.5H), 2.10 – 2.02 (m, 0.5H), 1.54 (q, *J* = 7.5 Hz, 2H), 1.29 – 1.21 (m, 3H), 0.97 – 0.89 (m, 3H), 0.26 (s, 9H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 173.3, 168.3, 167.8, 165.9, 99.9, 99.2, 59.4, 59.2, 40.3, 35.2, 20.4, 20.0, 14.6, 14.5, 13.85, 13.69, 0.8, 0.3. The physical and spectral data were consistent with those previously reported.[119]

Dimethyl 3-((trimethylsilyl)oxy)pent-2-enedioate, 2e

Yield 97 % (2.39 g, 9.7 mmol). Slightly yellow oil. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 5.22 (s, 1H), 3.81 (s, 2H), 3.69 (s, 3H), 3.65 (s, 3H), 0.27 (s, 9H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 169.8, 167.9, 164.7, 100.8, 52.1, 51.1, 39.8, 0.1. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{10}H_{18}SiNaO_5]^+$: 269.0816. Found: 269.0818.

Ethyl 2-benzyl-3-((trimethylsilyl)oxy)but-2-enoate, 2q

Yield 92 % (2.69 g, 9.2 mmol). Slightly yellow oil. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.29 – 7.09 (m, 5H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.66 (s, 2H), 2.36 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.22 (s, 9H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 169.4, 162.5, 142.1, 128.5, 128.1, 125.6, 113.0, 59.9, 32.5, 21.6, 14.4, 1.1. The physical and spectral data were consistent with those previously reported. [118]

Procedure for the synthesis of ethyl 3-ethoxybut-2-enoate, 3a

H_2SO_4 (100 μL) was added to the mixture of ethyl acetoacetate (6.5 g, 50.0 mmol, 1.0 equiv.) and triethyl orthoformate (11.5 mL, 70.0 mmol, 1.4 equiv.) with stirring at 0-10 °C. The reaction

mixture was stirred over night at 20-25 °C. Anhydrous K_2CO_3 (300.0 mg) was added, reaction mixture was filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). Distillation of the remaining liquid under medium vacuum (10 mmHg) gave product **3a** bp = 83-85 °C (10 mmHg). Yield 77 % (6.1 g, 38.6 mmol). Colorless oil. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.95 (s, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.78 (q, *J* = 7.0 Hz, 2H), 2.25 (s, 3H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). The physical and spectral data were consistent with those previously reported.[120]

General Procedure for the synthesis of enol ethers 3g, 3q[121]

A solution of **1** (192.2-220.0 mg, 1.0 mmol, 1.0 equiv.), $Cu(OAc)_2 \cdot H_2O$ (10.0 mg, 0.05 mmol, 0.05 equiv.) in 1,4-dioxane (2 mL) was stirred at room temperature. To the reaction mixture, a 5–6M TBHP solution in decane (2.2 mmol, 2.2 equiv.) was added dropwise. The reaction mixture was refluxed for 3 h. After cooling to room temperature, the reaction mixture was diluted EtOAc (50 mL), filtered through SiO_2 layer (2-3 cm). Filtrate was concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). The product **3** was isolated by column chromatography on SiO_2 (PE:EtOAc = from 15:1 to 1:1).

Ethyl 3-((1,4-dioxan-2-yl)oxy)-3-phenylacrylate, 3g

Yield 49 % (136.2 mg, 0.49 mmol). Yellow oil. R_f = 0.39 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.61 – 7.57 (m, 2H), 7.43 – 7.34 (m, 3H), 5.68 (s, 1H), 5.26 (t, *J* = 2.1 Hz, 1H), 4.39 – 4.29 (m, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.02 (dd, *J* = 12.0, 2.1 Hz, 1H), 3.84 – 3.67 (m, 3H), 3.49 (dt, *J* = 11.6, 2.9 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 165.2, 165.0, 135.3, 130.4, 128.7, 127.7, 103.7, 96.1, 68.3, 66.1, 61.8, 60.0, 14.5. The physical and spectral data were consistent with those previously reported.[121]

Ethyl 3-((1,4-dioxan-2-yl)oxy)-2-benzylbut-2-enoate, 3q.

Yield 55 % (168.5 mg, 0.55 mmol). Colorless oil. R_f = 0.33 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.33 – 7.11 (m, 5H), 5.10 (t, *J* = 2.4 Hz, 1H), 4.18 – 4.08 (m, 2H), 3.82 – 3.52 (m, 8H), 2.07 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 167.9,

157.8, 139.8, 128.5, 128.2, 126.2, 114.6, 94.4, 68.4, 66.1, 61.7, 60.4, 34.7, 16.3, 14.3. The physical and spectral data were consistent with those previously reported.[121]

General Procedure for the synthesis of enol acetates 4g, 4n, 4q

Acetyl chloride (535 μL, 588.8 mg, 7.5 mmol, 1.5 equiv.) was added to a solution of **1** (0.96-1.15 g, 5.0 mmol, 1.0 equiv.) in anhydrous pyridine (10 mL). The mixture was stirred at room temperature until the complete disappearance of **1**. The solution was then diluted with Et_2O (25 mL), washed with an aqueous saturated solution of $CuSO_4$ (2×25 mL), with H_2O (25 mL), dried over $MgSO_4$ and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). The product **4** was isolated by column chromatography on SiO_2 (PE:EtOAc = from 20:1 to 2:1).

Ethyl 3-acetoxy-3-phenylacrylate, 4g.[122]

Yield 38 % (445.0 mg, 1.9 mmol). Colorless oil. R_f = 0.37 (PE:EtOAc = 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.62 – 7.54 (m, 2H), 7.47 – 7.36 (m, 3H), 6.27 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 168.2, 164.3, 158.1, 133.5, 131.1, 128.9, 126.1, 106.3, 60.4, 21.1, 14.4. The physical and spectral data were consistent with those previously reported.[122]

Diethyl 2-(1-acetoxyethylidene)pentanedioate, 4n

Yield 78 % (1.06 g, 3.9 mmol). Colorless oil. R_f = 0.41 (PE:EtOAc = 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.20 (q, *J* = 7.1 Hz, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.58 – 2.49 (m, 2H), 2.41 – 2.32 (m, 2H), 2.25 (s, 3H), 2.18 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 173.0, 168.3, 167.1, 157.7, 120.9, 60.8, 60.5, 33.3, 23.0, 21.0, 19.6, 14.3. HRMS (ESI-TOF) m/z $[M+H]^+$. Calcd for $[C_{13}H_{21}O_6]^+$: 273.1333. Found: 273.1332.

Ethyl 3-acetoxy-2-benzylbut-2-enoate, 4q.[123]

Yield 50 % (656.0 mg, 2.5 mmol). Colorless oil. R_f = 0.54 (PE:EtOAc = 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.32 – 7.11 (m, 5H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.61 (s, 2H), 2.34 (s, 3H), 2.16 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 168.1, 167.3, 157.2, 139.4,

128.5, 128.4, 126.2, 121.6, 60.8, 33.2, 21.0, 19.5, 14.2. HRMS (ESI-TOF) m/z $[M+H]^+$. Calcd for $[C_{15}H_{19}O_4]^+$: 263.1278. Found: 263.1269. The physical and spectral data were consistent with those previously reported.[123]

General Procedure for the synthesis of acetals 5j, 5o, 5q

Toluene (20 mL) was added to **1** (0.85-1.10 g, 5.0 mmol, 1.0 equiv.), and then ethylene glycol (620.7 mg, 10.0 mmol, 2.0 equiv.) and *p*-toluenesulfonic acid monohydrate (190.2 mg, 1.0 mmol, 0.2 equiv.) were added to the reaction mixture. The mixture was refluxed for 2 h with water removal by means of Dean–Stark apparatus. Then, the mixture was added to a separatory funnel, and washed with water (5 mL), 10% Na_2CO_3 (5 mL) and brine (5 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). The product **5** was isolated by column chromatography on SiO_2 (PE:EtOAc = from 20:1 to 2:1).

Ethyl 1,4-dioxaspiro[4.5]decane-6-carboxylate, 5j[124]

Yield 80 % (0.85 g, 4.0 mmol). Colorless oil. R_f = 0.61 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.12 (q, *J* = 7.1 Hz, 2H), 3.99 – 3.82 (m, 4H), 2.64 (dd, *J* = 8.1, 5.5 Hz, 1H), 1.95 – 1.79 (m, 3H), 1.73 – 1.55 (m, 3H), 1.53 – 1.39 (m, 1H), 1.36 – 1.21 (m, 4H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 172.5, 108.8, 65.0, 64.6, 60.4, 50.1, 34.8, 27.4, 23.5, 23.1, 14.3. The physical and spectral data were consistent with those previously reported.[124]

Ethyl 4-cyano-2-(2-methyl-1,3-dioxolan-2-yl)butanoate, 5o

Yield 67 % (0.76 g, 3.3 mmol). Colorless oil. R_f = 0.69 (PE:EtOAc = 1:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.18 (q, *J* = 7.1 Hz, 2H), 4.03 – 3.90 (m, 4H), 2.76 (dd, *J* = 9.9, 4.8 Hz, 1H), 2.48 – 2.24 (m, 2H), 2.16 – 1.94 (m, 2H), 1.38 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 171.4, 119.0, 109.1, 64.99, 64.86, 61.1, 52.7, 24.0, 21.7, 15.8, 14.2.

Ethyl 2-(2-methyl-1,3-dioxolan-2-yl)-3-phenylpropanoate, 5q. [125]

Yield 88 % (1.16 g, 4.4 mmol). Colorless oil. R_f = 0.48 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.31 – 7.12 (m, 5H), 4.11 – 3.98 (m, 6H), 3.09 – 2.93 (m, 3H), 1.49 (s, 3H), 1.08 (t, *J* =

7.1 Hz, 3H). $^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 172.1, 139.4, 128.9, 128.5, 126.4, 109.6, 65.1, 65.0, 60.5, 56.5, 34.4, 21.9, 14.2. The physical and spectral data were consistent with those previously reported.[126]

Synthesis of disubstituted β-ketoesters 8a-c

Procedure for the synthesis of ethyl 2,2-dimethyl-3-oxobutanoate, 8a

Ethyl acetoacetate (1.30 g, 10.0 mmol, 1.0 equiv.) was added to a suspension of K_2CO_3 (5.52 g, 40.0 mmol, 4.0 equiv.) in anhydrous DMSO (8 mL). Later, methyl iodide (5.68 g, 40.0 mmol, 4.0 equiv.) and dibenzo-18-crown-6 (100 mg) were added with stirring. The mixture was stirred at 20-25 °C overnight until the complete disappearance of ethyl acetoacetate. The reaction mixture was then diluted with H_2O (50 mL), extracted with Et_2O (3×20 mL). Combined organic layers were washed with brine (3×10 mL), dried over $MgSO_4$ and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). The product **8a** was isolated by column chromatography on SiO_2 (PE:EtOAc = from 20:1 to 5:1). Yield 53 % (838.0 mg, 5.3 mmol). Colorless oil. R_f = 0.69 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 4.18 (q, J = 7.1 Hz, 2H), 2.14 (s, 3H), 1.35 (s, 6H), 1.25 (t, J = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 206.0, 173.7, 61.4, 55.9, 25.8, 22.0, 14.1. The physical and spectral data were consistent with those previously reported.[127]

Procedure for the synthesis of ethyl 2-benzyl-2-methyl-3-oxobutanoate, 8b

Ethyl 2-benzyl-3-oxobutanoate **1q** (1.10 g, 5.0 mmol, 1.0 equiv.) was added to a suspension of K_2CO_3 (2.76 g, 20.0 mmol, 4.0 equiv.) in anhydrous DMSO (5 mL). Later, methyl iodide (1.42 g, 10.0 mmol, 2.0 equiv.) and dibenzo-18-crown-6 (50 mg) were added with stirring. The mixture was stirred at 20-25 °C overnight until the complete disappearance of ethyl 2-benzyl-3-oxobutanoate **1q**. The reaction mixture was then diluted with H_2O (20 mL), extracted with Et_2O (3×10 mL). Combined organic layers were washed with brine (3×5 mL), dried over $MgSO_4$ and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). The product **8b** was isolated by column chromatography on SiO_2 (PE:EtOAc =

from 20:1 to 5:1). Yield 84 % (984.0 mg, 4.2 mmol). Colorless oil. R_f = 0.76 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.30 – 7.17 (m, 3H), 7.09 (d, *J* = 7.6 Hz, 2H), 4.31 – 4.02 (m, 2H), 3.27 (d, *J* = 13.8 Hz, 1H), 3.05 (d, *J* = 13.8 Hz, 1H), 2.16 (s, 3H), 1.28 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 205.5, 172.6, 136.6, 130.3, 128.3, 127.0, 61.5, 61.0, 40.6, 26.6, 19.2, 14.1. The physical and spectral data were consistent with those previously reported.[128]

Procedure for the synthesis of ethyl 2,2-dibenzyl-3-oxobutanoate, 8c

Ethyl acetoacetate (1.30 g, 10.0 mmol, 1.0 equiv.) was added to a suspension of K_2CO_3 (5.52 g, 40.0 mmol, 4.0 equiv.) in anhydrous DMSO (8 mL). Later, benzyl bromide (6.84 g, 40.0 mmol, 4.0 equiv.), KI (50 mg) and dibenzo-18-crown-6 (100 mg) were added with stirring. The mixture was stirred at 20-25 °C overnight until the complete disappearance of ethyl acetoacetate. The reaction mixture was then diluted with H_2O (50 mL), extracted with Et_2O (3×20 mL). Combined organic layers were washed with brine (3×10 mL), dried over $MgSO_4$ and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 40–45 °C). The product **8c** was isolated by column chromatography on SiO_2 (PE:EtOAc = from 20:1 to 5:1). Yield 41 % (1.28 g, 4.1 mmol). Colorless oil. R_f = 0.58 (PE:EtOAc = 10:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.30 – 7.19 (m, 6H), 7.17 – 7.07 (m, 4H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.22 (s, 4H), 1.96 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 205.7, 171.9, 136.5, 130.2, 128.4, 127.0, 66.3, 61.4, 40.0, 29.2, 14.0. The physical and spectral data were consistent with those previously reported.[127]

Experimental Procedure for Table 1

Experimental Procedure for Table 1, entries 1-9

An ethereal solution of H_2O_2 (2.048 M, 0.488-4.882 mL, 1.00-10.00 mmol, 1-10 equiv.) was added with stirring to **1q** (220.3 mg, 1.00 mmol, 1.0 equiv.). Later, $BF_3{\cdot}Et_2O$ (141.9 mg - 1.419 g, 1.00-10.00 mmol, 1-10 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 1, 3, or 12 h. After that time, CH_2Cl_2 (40 mL) and

H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **6q** was isolated by chromatography on SiO_2 with elution using PE-EtOAc mixture (5:1).

Experimental Procedure for Table 1, entry 10

Urea hydrogen peroxide (940.0 mg, 10.00 mmol, 10.0 equiv.) was added with stirring to a solution of **1q** (220.3 mg, 1.00 mmol, 1.0 equiv.) in Et_2O (4.9 mL). Later, $BF_3 \cdot Et_2O$ (1.419 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 24 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **6q** was isolated as described above. Yield of **6q** was 43 % (96.4 mg, 0.43 mmol).

Experimental Procedure for Table 1, entries 11, 12

Ethyl 2-benzyl-3-oxobutanoate **1q** (220.3 mg, 1.00 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (0.6 mL) and one drop of 5% aq. H_2SO_4 (0.3 μL) was added. H_2O_2 (90%, 150.0 mg, 4.00 mmol, 4.0 equiv.) was added dropwise with stirring to the solution at 20°C. The reaction mixture was then cooled to 0°C and 50% aq. H_2SO_4 (34-719 μL, 0.24-10.00 mmol, 0.24-10.0 equiv.) was added dropwise. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (50 mL) was added and the organic layer was washed with brine (10 mL), a 5% aqueous $NaHCO_3$ solution (2 × 10 mL), and again with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Traces of target product **6q** were detected by ^1H NMR after the synthesis.

Experimental Procedure for Table 1, entries 13-17

An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10 equiv.) was added with stirring to **1q** (220.3 mg, 1.00 mmol, 1.0 equiv.). Later, H_2SO_4 (980.0 mg, 10.00 mmol, 10 equiv.), or 70%

aq. $HClO_4$ (1.435 g, 10.00 mmol, 10 equiv.), or 48% aq. HBF_4 (1.829 g, 10.00 mmol, 10 equiv.), or PMA (2340.0 mg, 1.00 mmol, 1.0 equiv.), or PTA (3249.5 mg, 0.50 mmol, 0.5 equiv.) was added with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 or 24 h. After that time, CH_2Cl_2 (50 mL) was added and the organic layer was washed with brine (10 mL), a 5% aqueous $NaHCO_3$ solution (2 × 10 mL), and again with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **6q** was isolated as described above.

Experimental Procedure for Table 1, entries 18-20

An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.0 mmol, 10.0 equiv.) was added with stirring to **1q** (220.3 mg, 1.00 mmol, 1.0 equiv.). Later, $Na_2MoO_4 \cdot 2H_2O$ (483.8 mg, 2.00 mmol, 2.0 equiv.), or I_2 (25.4-1270.0 mg, 0.10-5.00 mmol, 0.1-5.0 equiv.) was added with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 24 h. Target product **6q** was not detected by TLC during the reaction and after the synthesis.

Experimental Procedure for Table 1, entry 21

An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) was added with stirring to **1q** (220.3 mg, 1.00 mmol, 1.0 equiv.). Later, TBAI (738.7 mg, 2.00 mmol, 2.0 equiv.) was added with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 24 h. Later, Et_2O (50 mL) was added. Reaction mixture was filtered of through SiO_2 (2-3 cm) and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **6q** was not detected. By-product 4-phenylbutan-2-one (**7**) was isolated by chromatography on SiO_2 with elution using PE-EtOAc mixture (5:1). Yield of **7** was 27 % (40.0 mg, 0.27 mmol).

4-Phenylbutan-2-one, 7

Colorless oil. R_f = 0.68 (PE:EtOAc = 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.31 – 7.25 (m, 2H), 7.23 – 7.15 (m, 3H), 2.90 (t, *J* = 7.4 Hz, 2H), 2.76 (t, *J* = 7.4 Hz, 2H), 2.14 (s, 3H).

$^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 208.0, 141.1, 128.6, 128.4, 126.2, 45.3, 30.2, 29.9. The physical and spectral data were consistent with those previously reported.[129]

Experimental Procedure for Table 2

Procedure for experiments in optimal conditions for β-ketoesters "Substrate/H_2O_2/BF_3·Et_2O" (first column)

An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) was added with stirring to enol ether **2q**-**4q** or acetal **5q** (262.3-306.4 mg, 1.00 mmol, 1.0 equiv.). Later, BF_3·Et_2O (1.419 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **6q** was isolated as described above.

Procedure for experiments with other order of addition of reagents "H_2O_2/BF_3·Et_2O/ Substrate" (second column)

BF_3·Et_2O (1.419 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to an ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) at 0°C. Later, enol ether **2q**-**4q** or acetal **5q** (262.3-306.4 mg, 1.00 mmol, 1.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **6q** was isolated as described above.

Procedure for experiments with other order of addition of reagents and with $HClO_4$ instead of BF_3·Et_2O "H_2O_2/$HClO_4$/ Substrate" (third column)

70 % aq. $HClO_4$ (1.435 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to an ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) at 0°C. Later, enol ether **2q**-**4q** or acetal **5q** (262.3-306.4 mg, 1.00 mmol, 1.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (50 mL) was added and the organic layer was washed with brine (10 mL), a 5% aqueous $NaHCO_3$ solution (2 × 10 mL), and again with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **6q** was isolated as described above.

General Experimental Procedure for Table 3

An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) was added with stirring to **1a-u** (130.1-327.2 mg, 1.00 mmol, 1.0 equiv.). Later, $BF_3 \cdot Et_2O$ (1.419 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **6** was isolated by chromatography on SiO_2 (PE-EtOAc = from 5:1 to 2:1).

5-Hydroperoxy-5-methyl-1,2-dioxolan-3-one, 6a

Yield was 88% (118.0 mg, 0.88 mmol) from ethyl acetoacetate (**1a**) and 89% (119.3 mg, 0.89 mmol) from ethyl 3-ethoxybut-2-enoate (**3a**). Colorless oil. R_f = 0.47 (PE:EtOAc =5:1).

^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 9.17 (s, 1H), 3.22 (d, *J* = 17.8 Hz, 1H), 3.13 (d, *J* = 17.8 Hz, 1H), 1.67 (s, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 173.7, 113.8, 39.6, 18.5. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_4H_6NaO_5]^+$: 157.0107. Found: 157.0112. Anal. Calcd for $C_4H_6O_5$: C, 35.83; H, 4.51. Found: C, 35.77; H, 4.49. IR (thin layer): 3207, 2837, 1804, 1625, 1404, 1383, 1323, 1238, 1196, 1116, 1079, 837, 814 cm^{-1}.

5-Hydroperoxy-5-propyl-1,2-dioxolan-3-one, 6b

Yield was 96% (155.6 mg, 0.96 mmol) from **1b** and 88% (142.6 mg, 0.88 mmol) from **2b**. Colorless oil. R_f = 0.46 (PE:EtOAc =4:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.85 (s, 1H), 3.19 (d, *J* = 17.8 Hz, 1H), 3.05 (d, *J* = 17.8 Hz, 1H), 2.06 – 1.92 (m, 1H), 1.87 – 1.73 (m, 1H), 1.61 – 1.34 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 173.6, 115.9, 38.2, 33.9, 17.7, 14.0. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_6H_{10}NaO_5]^+$: 185.0420. Found: 185.0423. Anal. Calcd for $C_6H_{10}O_5$: C, 44.45; H, 6.22. Found: C, 44.35; H, 6.31. IR (thin layer): 2970, 2940, 2879, 1804, 1467, 1404, 1329, 1203, 1121, 972, 833, 540 cm^{-1}.

5-Hydroperoxy-5-isopropyl-1,2-dioxolan-3-one, **6c**

Yield 90% (145.9 mg, 0.90 mmol). White crystals, mp = 45-46 °C. R_f = 0.39 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.64 (s, 1H), 3.19 (d, *J* = 17.8 Hz, 1H), 3.02 (d, *J* = 17.8 Hz, 1H), 2.33 (sept, *J* = 7.0 Hz, 1H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 173.4, 118.3, 35.6, 31.6, 17.8, 17.3. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_6H_{10}NaO_5]^+$: 185.0420. Found: 185.0417. Anal. Calcd for $C_6H_{10}O_5$: C, 44.45; H, 6.22 %. Found: C, 44.32; H, 6.19. IR (KBr): 3325, 3019, 2980, 1794, 1473, 1436, 1402, 1218, 1196, 1071, 990, 866, 593, 499 cm^{-1}.

5-Hydroperoxy-5-isobutyl-1,2-dioxolan-3-one, 6d

Yield 64% (112.7 mg, 0.64 mmol). White crystals, mp = 46-47 °C. R_f = 0.31 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.82 (s, 1H), 3.20 (d, *J* = 17.7 Hz, 1H), 3.09 (d, *J* = 17.7 Hz, 1H), 2.02 – 1.81 (m, 2H), 1.70 (dd, *J* = 14.0, 7.2 Hz, 1H), 1.02 – 0.94 (m, 6H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 173.5, 115.7, 40.6, 39.0, 24.6, 23.5, 23.2. HRMS (ESI-TOF) m/z $[M+H]^+$. Calcd for $[C_7H_{13}O_5]^+$: 177.0757. Found: 177.0754. Anal. Calcd for $C_7H_{12}O_5$: C, 47.73; H, 6.87. Found: C, 47.81; H, 6.83. IR (KBr): 3361, 2963, 2875, 2339, 1806, 1601, 1402, 1371, 1205, 1123, 977, 859, 593 cm^{-1}.

Methyl 2-(3-hydroperoxy-5-oxo-1,2-dioxolan-3-yl)acetate, 6e

Yield was 79% (151.8 mg, 0.79 mmol) from **1e** and 61% (117.1 mg, 0.61 mmol) from **2e**. Colorless oil. R_f = 0.43 (PE:EtOAc =2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 9.42 (s, 1H), 3.76 (s, 3H), 3.66 (d, *J* = 16.8 Hz, 1H), 3.19 (d, *J* = 16.8 Hz, 1H), 3.13 (d, *J* = 14.6 Hz, 1H), 2.97 (d, *J* = 14.6 Hz, 1H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 172.7, 167.8, 112.8, 52.9, 38.2, 36.2. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_6H_8NaO_7]^+$: 215.0162. Found: 215.0165. Anal. Calcd for $C_6H_8O_7$: C, 37.51; H, 4.20. Found: C, 37.18; H, 4.30. IR (film): 3178, 2958, 2833, 2340, 1805, 1732, 1587, 1371, 1227, 1003, 837, 669 cm^{-1}.

Ethyl 2-(3-hydroperoxy-5-oxo-1,2-dioxolan-3-yl)acetate, 6f

Yield 78% (160.8 mg, 0.78 mmol). Colorless oil. R_f = 0.43 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 9.36 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.67 (d, *J* = 18.2 Hz, 1H), 3.18 (d, *J* = 18.2 Hz, 1H), 3.12 (d, *J* = 16.1 Hz, 1H), 2.96 (d, *J* = 16.1 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 172.8, 167.3, 112.8, 62.1, 38.2, 36.4, 14.1. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_7H_{10}NaO_7]^+$: 229.0319. Found: 229.0329. Anal. Calcd for $C_7H_{10}O_7$: C, 40.78; H, 4.89. Found: C, 40.82; H, 5.02. IR (thin layer): 2987, 2340, 1806, 1732, 1633, 1401, 1377, 1231, 1185, 1026, 837, 694 cm^{-1}.

5-Hydroperoxy-5-phenyl-1,2-dioxolan-3-one, 6g

Yield was 61% (119.6 mg, 0.61 mmol) from **1g**, 73% (143.1 mg, 0.73 mmol) from **3g** and 86% (168.6 mg, 0.86 mmol) from **4g**. Colorless oil. R_f = 0.51 (PE:EtOAc =7:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 9.01 (s, 1H), 7.57 – 7.43 (m, 5H), 3.41 (s, 2H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 172.8, 132.4, 130.6, 129.1, 126.2, 114.5, 41.3. HRMS (ESI-TOF) m/z $[M+H]^+$. Calcd for $[C_9H_9O_5]^+$: 197.0444. Found: 197.0446.

5-Benzyl-5-hydroperoxy-1,2-dioxolan-3-one, 6h

Yield 77% (161.0 mg, 0.77 mmol). White crystals, mp = 93-94 °C. R_f = 0.24 (PE:EtOAc =2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.75 (s, 1H), 7.49 – 7.18 (m, 5H), 3.27 (d, *J* = 14.7 Hz, 1H), 3.19 (d, *J* = 14.7 Hz, 1H), 3.11 (d, *J* = 17.8 Hz, 1H), 2.84 (d, *J* = 17.8 Hz, 1H). ^{13}C{^{1}H}NMR (75.48

MHz, $CDCl_3$, δ): 172.8, 133.1, 130.3, 129.1, 128.1, 115.9, 37.7, 37.4. Anal. Calcd for $C_{10}H_{10}O_5$: C, 57.14; H, 4.80. Found: C, 57.41; H, 4.75. IR (KBr): 3335, 3021, 2947, 2338, 1795, 1731, 1498, 1442, 1401, 1183, 1087, 982, 859, 812, 703, 602, 489 cm^{-1}.

6a-Hydroperoxytetrahydrocyclopenta[*c*][1,2]dioxol-3(3a*H*)-one, 6i

Yield 87% (139.3 mg, 0.87 mmol). Colorless oil. R_f = 0.40 (PE:EtOAc =2:1). ^1H NMR (300.13 MHz, $CDCl_3$, δ): 9.17 (s, 1H), 3.56 (dd, *J* = 10.7, 4.4 Hz, 1H), 2.37 – 1.99 (m, 6H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 177.0, 126.1, 49.3, 34.9, 29.0, 25.5. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_6H_8NaO_5]^+$: 183.0264. Found: 183.0256. Anal. Calcd for $C_6H_8O_5$: C, 45.01; H, 5.04. Found: C, 45.14; H, 5.37. IR (thin layer): 3236, 2975, 1796, 1738, 1439, 1331, 1207, 1115, 944, 807, 661 cm^{-1}.

7a-Hydroperoxyhexahydro-3*H*-benzo[*c*][1,2]dioxol-3-one, 6j

Yield was 57% (100.0 mg, 0.57 mmol) from **1j** and 75% (130.6 mg, 0.75 mmol) from **5j**. Colorless oil. R_f = 0.25 (PE:EtOAc =5:1). ^1H NMR (300.13 MHz, $CDCl_3$, δ): 8.74 (s, 1H), 2.86 – 2.75 (m, 1H), 2.35 – 2.22 (m, 2H), 1.89 – 1.24 (m, 6H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 176.2, 113.7, 44.2, 27.1, 25.8, 22.5, 21.6. HRMS (APCI-TOF) m/z $[M+H]^+$. Calcd for $[C_7H_{11}O_5]^+$: 175.0601. Found: 175.0609. Anal. Calcd for $C_7H_{10}O_5$: C, 48.28; H, 5.79. Found: C, 48.14; H, 5.47. IR (thin layer): 2960, 2874, 1707, 1453, 1418, 1286, 1231, 1197, 1174, 1095, 940, 656 cm^{-1}.

4-(Adamantan-1-yl)-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one, **6k**

Yield 80% (214.6 mg, 0.80 mmol). Colorless oil. R_f = 0.54 (PE:EtOAc =5:1). ^1H NMR (300.13 MHz, $CDCl_3$, δ): 8.55 (s, 1H), 2.76 (s, 1H), 2.08 – 1.97 (m, 6H), 1.80 – 1.68 (m, 12H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 173.1, 116.1, 59.9, 39.8, 36.7, 34.5, 28.5, 19.7. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{14}H_{20}NaO_5]^+$: 291.1203. Found: 291.1204. Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.70; H, 7.58. IR (KBr): 3316, 2917, 2850, 1763, 1443, 1259, 1172, 1123, 867, 655, 579, 502 cm^{-1}.

5-Hydroperoxy-5-methyl-4-(prop-2-yn-1-yl)-1,2-dioxolan-3-one, 6l

Yield 64% (110.2 mg, 0.64 mmol). White crystals, mp = 60-61 °C. R_f = 0.37 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.61 (s, 1H), 3.30 (dd, *J* = 10.3, 4.7 Hz, 1H), 2.87 – 2.66 (m, 2H), 2.12 (t, *J* = 2.5 Hz, 1H), 1.78 (s, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 173.7, 114.1, 79.1, 71.2, 48.1, 18.8, 14.5. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_7H_8NaO_5]^+$: 195.0264. Found: 195.0261. Anal. Calcd for $C_7H_8O_5$: C, 48.84; H, 4.68. Found: C, 48.93; H, 4.56. IR (KBr): 3296, 2340, 1794, 1608, 1426, 1382, 1354, 1275, 1249, 1192, 1123, 1094, 916, 839, 682, 665, 557 cm^{-1}.

Ethyl 2-(3-hydroperoxy-3-methyl-5-oxo-1,2-dioxolan-4-yl)acetate, 6m

Yield 73% (160.7 mg, 0.73 mmol). Colorless oil. R_f = 0.32 (PE:EtOAc =4:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 9.39 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.75 (dd, *J* = 7.8, 4.9 Hz, 1H), 3.01 – 2.76 (m, 2H), 1.63 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 174.7, 171.0, 114.2, 61.9, 45.6, 29.7, 18.4, 14.2. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_8H_{12}NaO_7]^+$: 243.0475. Found: 243.0475. Anal. Calcd for $C_8H_{12}O_7$: C, 43.64; H, 5.49. Found: C, 43.49; H, 5.80. IR (thin layer): 3352, 2987, 2938, 2875, 2340, 1802, 1732, 1657, 1415, 1383, 1276, 1176, 1122, 1092, 1025, 866, 844, 578 cm^{-1}.

Ethyl 3-(3-hydroperoxy-3-methyl-5-oxo-1,2-dioxolan-4-yl)propanoate, 6n

Yield was 66% (154.0 mg, 0.66 mmol) from **1n** and 30% (70.3 mg, 0.30 mmol) from **4n**. Colorless oil. R_f = 0.57 (PE:EtOAc =2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 9.09 (s, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.30 (dd, *J* = 8.4, 5.8 Hz, 1H), 2.75 – 2.59 (m, 2H), 2.22 – 2.02 (m, 2H), 1.67 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 175.5, 173.1, 114.5, 61.1, 47.7, 30.2, 19.6, 18.2, 14.3. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_9H_{14}NaO_7]^+$: 257.0632. Found: 257.0633. Anal. Calcd for $C_9H_{14}O_7$: C, 46.16; H, 6.03. Found: C, 46.11; H, 6.08. IR (thin layer): 3346, 2987, 1801, 1714, 1382, 1198, 1086, 1026, 858, 839, 582 cm^{-1}.

3-(3-Hydroperoxy-3-methyl-5-oxo-1,2-dioxolan-4-yl)propanenitrile, 6o

Yield was 78% (146.0 mg, 0.78 mmol) from **1o** and 74% (138.5 mg, 0.74 mmol) from **5o**. White crystals, mp = 42-43 °C. R_f = 0.28 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 9.24 (s, 1H), 3.25 (dd, *J* = 8.7, 5.8 Hz, 1H), 2.88 – 2.65 (m, 2H), 2.35 – 2.23 (m, 1H), 2.14 – 2.00 (m, 1H), 1.67 (s, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 174.7, 118.6, 114.1, 47.3, 20.8, 18.2, 14.6. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_7H_9NNaO_5]^+$: 210.0373. Found: 210.0378. Anal. Calcd for $C_7H_9NO_5$: C, 44.92; H, 4.85; N, 7.48. Found: C, 45.03; H, 5.02; N, 7.49. IR (KBr): 3397, 2340, 2251, 1800, 1719, 1586, 1425, 1384, 1242, 1176, 1127, 1086, 862, 838, 658 cm^{-1}.

4-(3,3-Dihydroperoxybutyl)-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one, 6p

Yield 56% (142.3 mg, 0.56 mmol). White crystals, mp = 101-102 °C. R_f = 0.32 (PE:EtOAc =2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.94 (s, 1H), 8.27 (s, 2H), 3.24 (dd, *J* = 8.4, 1.9 Hz, 1H), 2.41 – 2.28 (m, 1H), 2.19 – 2.01 (m, 2H), 1.89 – 1.79 (m, 1H), 1.63 (s, 3H), 1.44 (s, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 175.1, 115.1, 112.6, 45.4, 28.5, 18.0, 17.9, 17.8. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_8H_{14}NaO_9]^+$: 277.0530. Found: 277.0531. Anal. Calcd for $C_8H_{14}O_9$: C, 37.80; H, 5.55. Found: C, 37.51; H, 5.61. IR (KBr): 3392, 1794, 1785, 1459, 1382, 1320, 1235, 1194, 1103, 941, 863, 846, 830, 757, 570, 532 cm^{-1}.

4-Benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one, 6q

Yield 92% (206.3 mg, 0.92 mmol). White crystals, mp = 110-111 °C. R_f = 0.53 (PE:EtOAc =2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.67 (s, 1H), 7.39 – 7.22 (m, 5H), 3.40 – 3.23 (m, 2H), 3.05 (dd, *J* = 13.8, 9.9 Hz, 1H), 1.20 (s, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 175.0, 136.9, 129.2, 128.9, 127.3, 114.3, 51.3, 30.7, 18.4. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{11}H_{12}NaO_5]^+$: 247.0577. Found: 247.0581. Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 59.03; H, 5.02. IR (KBr): 3294, 2900, 1800, 1768, 1603, 1274, 1213, 1178, 1086, 844, 749, 698 cm^{-1}.

4-(4-(*Tert*-butyl)benzyl)-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one, 6r

Yield 76% (213.0 mg, 0.76 mmol). White crystals, mp = 123-124 °C. R_f = 0.58 (PE:EtOAc =2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.77 (s, 1H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 3.38 – 3.20 (m, 2H), 3.02 (dd, *J* = 14.4, 10.1 Hz, 1H), 1.32 (s, 9H), 1.23 (s, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 175.1, 150.3, 133.8, 128.9, 125.8, 114.4, 51.3, 34.6, 31.5, 30.1, 18.4. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{15}H_{20}NaO_5]^+$: 303.1203. Found: 303.1193. Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.30; H, 7.03. IR (KBr): 3379, 2971, 2953, 1780, 1414, 1267, 1221, 1103, 838, 566 cm^{-1}.

4-(4-Chlorobenzyl)-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one, 6s

Yield 93% (240.5 mg, 0.93 mmol). White crystals, mp = 108 °C. R_f = 0.29 (PE:EtOAc =2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.79 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 3.35 – 3.18 (m, 2H), 3.03 (dd, *J* = 13.7, 9.5 Hz, 1H), 1.23 (s, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 174.7, 135.3, 133.2, 130.6, 129.1, 114.2, 51.1, 30.1, 18.5. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{11}H_{11}ClNaO_5]^+$: 281.0187. Found: 281.0177. Anal. Calcd for $C_{11}H_{11}ClO_5$: C, 51.08; H, 4.29; Cl, 13.71. Found: C, 51.09; H, 4.22; Cl, 13.75. IR (KBr): 3293, 2789, 2339, 1793, 1764, 1493, 1408, 1335, 1272, 1234, 1212, 1175, 1100, 1020, 925, 842, 825, 779, 626, 594, 552, 409 cm^{-1}.

4-(4-Bromobenzyl)-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one, 6t

Yield was 81% (245.5 mg, 0.81 mmol) from *tert*-butyl 2-(4-bromobenzyl)-3-oxobutanoate (**1t**). White crystals, mp = 119 °C. R_f = 0.22 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.59 (s, 1H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 3.33 – 3.17 (m, 2H), 3.01 (dd, *J* = 14.2, 10.0 Hz, 1H), 1.24 (s, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 174.6, 135.8, 132.1, 131.0, 121.3, 114.1, 51.0, 30.2, 18.6. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{11}H_{11}BrNaO_5]^+$: 324.9682, 326.9662. Found: 324.9675, 326.9659. Anal. Calcd for $C_{11}H_{11}BrO_5$: C, 43.59; H, 3.66; Br, 26.36. Found: C, 43.61; H, 3.64; Br, 26.17. IR (KBr): 3285, 2797, 1790, 1766, 1489, 1407, 1234, 1212, 1176, 1091, 1072, 1017, 926, 841, 822, 653, 552 cm^{-1}.

4-Benzyl-5-hydroperoxy-5-propyl-1,2-dioxolan-3-one, 6u

Yield 90% (227.0 mg, 0.90 mmol). Colorless oil. R_f = 0.61 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.53 (s, 1H), 7.38 – 7.27 (m, 5H), 3.42 – 3.25 (m, 2H), 3.07 (dd, *J* = 14.2, 9.1 Hz, 1H), 1.64 – 1.53 (m, 1H), 1.34 – 1.05 (m, 3H), 0.72 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 175.2, 137.2, 129.2, 128.9, 127.3, 116.4, 48.6, 33.7, 30.9, 17.0, 14.0. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{13}H_{16}NaO_5]^+$: 275.0890. Found: 275.0894. Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.92; H, 6.28. IR (KBr): 3286, 3033, 2968, 2871, 1788, 1758, 1458, 1418, 1337, 1268, 1201, 1169, 1121, 1085, 1029, 941, 934, 840, 749, 696, 603 cm^{-1}.

General Experimental Procedure for Scheme 4

An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) was added with stirring to **8** (158.2-310.4 mg, 1.00 mmol, 1.0 equiv.). Later, $BF_3 \cdot Et_2O$ (1.419 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **9** was isolated by chromatography on SiO_2 (PE:EtOAc = 6:1).

5-Hydroperoxy-4,4,5-trimethyl-1,2-dioxolan-3-one, 9a

Yield 86% (140.0 mg, 0.86 mmol). White crystals, mp = 88-89 °C. R_f = 0.47 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.48 (s, 1H), 1.54 (s, 3H), 1.38 (s, 3H), 1.26 (s, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 178.9, 116.5, 47.9, 22.7, 16.6, 13.8. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_6H_{10}NaO_5]^+$: 185.0420. Found: 185.0412. Anal. Calcd for $C_6H_{10}O_5$: C, 44.45; H, 6.22. Found: C, 44.51; H, 6.18. IR (KBr): 3354, 1793, 1772, 1420, 1379, 1274, 1164, 1141, 1123, 1095, 880, 843, 577 cm^{-1}.

4-Benzyl-5-hydroperoxy-4,5-dimethyl-1,2-dioxolan-3-one, 9b

Yield 74% (176.1 mg, 0.74 mmol). White crystals, mp = 76-77 °C. R_f = 0.67 (PE:EtOAc =5:1). **9b** was prepared as inseparable mixture of diastereomers, dr = 4/1. ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 8.56 (s, 0.8H), 8.45 (s, 0.2H), 7.42 – 7.24 (m, 4.6H), 7.18 – 7.08 (m, 0.4H), 3.28 (d, *J* = 14.1 Hz, 0.8H), 3.17 (d, *J* = 13.2 Hz, 0.2H), 2.91 – 2.74 (m, 1H), 1.68 (s, 0.6H), 1.35 (s, 2.4H), 1.19 (s, 3H). ^{13}C{^{1}H}NMR (75.48 MHz, $CDCl_3$, δ): 178.6, 134.1, 131.4, 130.7, 128.5, 128.4, 127.5, 116.4, 50.9, 36.2, 19.4, 14.5, 13.7. HRMS (ESI-TOF) m/z $[M+NH_4]^+$. Calcd for $[C_{12}H_{18}NO_5]^+$: 256.1179. Found: 256.1186. Anal. Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.59; H, 5.89. IR (KBr): 3418, 1781, 1454, 1376, 1246, 1162, 1107, 1089, 868, 765, 705, 506 cm^{-1}.

4,4-Dibenzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one, 9c

Product **9c** was not detected after synthesis. Starting compound **8c** was isolated 82% (253.0 mg, 0.82 mmol).

Experimental Procedures for Scheme 5

Synthesis of peroxide 10 by reaction of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one (6q) with 3,4-dihydro-2H-pyran (DHP).

p-TsOH·H_2O (19.0 mg, 0.10 mmol, 0.1 equiv.) was added with stirring to solution of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one **6q** (224.21 mg, 1.00 mmol, 1.0 eq) in CH_2Cl_2 (2 mL). Later, DHP (92.5 mg, 1.10 mmol, 1.1 equiv.) was added. The reaction mixture was stirred at 20-25 °C for 2 h. Later, CH_2Cl_2 (50 mL) was added and the organic layer was washed with 5% aqueous $NaHCO_3$ solution (2 × 10 mL), and with brine (5 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **10** (inseparable mixture of diastereomers (1:1)) was isolated by chromatography on SiO_2 (PE-EtOAc = 5:1).

4-Benzyl-5-methyl-5-((tetrahydro-2H-pyran-2-yl)peroxy)-1,2-dioxolan-3-one, 10

Yield 71% (218.9 mg, 0.71 mmol). Colorless oil. R_f = 0.43 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.39 – 7.22 (m, 5H), 5.40-5.43 (m, 0.5H), 5.31-5.34 (m, 0.5H), 4.14 – 4.00 (m, 1H), 3.76 – 3.65 (m, 1H), 3.38 – 3.15 (m, 2.5H), 2.99 (dd, *J* = 14.1, 10.3 Hz, 0.5H), 1.82 – 1.56

(m, 6H), 1.26 (s, 1.5H), 1.16 (s, 1.5H). $^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 175.1, 174.9, 137.2, 137.0, 129.31, 129.30, 128.91, 128.87, 127.2, 114.6, 113.4, 102.7, 101.4, 62.7, 62.5, 52.2, 51.2, 30.9, 30.6, 27.7, 27.6, 25.1, 19.4, 19.3, 18.7. HRMS (ESI-TOF) m/z $[M+NH_4]^+$. Calcd for $[C_{16}H_{24}NO_6]^+$: 326.1598. Found: 326.1596. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.38; H, 6.42. IR (thin layer): 3031, 2947, 2873, 1802, 1604, 1497, 1456, 1443, 1380, 1262, 1174, 1109, 1084, 1040, 962, 896, 875, 816, 751, 701, 553 cm^{-1}.

Synthesis of peroxide 11 by reaction of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one (6q) with 2,3-dihydrofuran (DHF).

p-TsOH·H_2O (19.0 mg, 0.10 mmol, 0.1 equiv.) was added with stirring to a solution of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one **6q** (224.21 mg, 1.00 mmol, 1.0 eq) in CH_2Cl_2 (2 mL). Later, DHF (77.1 mg, 1.10 mmol, 1.1 equiv.) was added. The reaction mixture was stirred at 20-25 °C for 2 h. Later, CH_2Cl_2 (50 mL) was added and the organic layer was washed with 5% aqueous $NaHCO_3$ solution (2 × 10 mL), and with brine (5 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **11** (inseparable mixture of diastereomers (1:1)) was isolated by chromatography on SiO_2 (PE-EtOAc = 5:1).

4-Benzyl-5-methyl-5-((tetrahydrofuran-2-yl)peroxy)-1,2-dioxolan-3-one, 11

Yield 70% (206.0 mg, 0.70 mmol). Colorless oil. R_f = 0.49 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.39 – 7.21 (m, 5H), 5.88 (dd, *J* = 6.1, 1.8 Hz, 0.5H), 5.80 – 5.70 (m, 0.5H), 4.09 – 3.97 (m, 2H), 3.33 – 2.96 (m, 3H), 2.18 – 1.74 (m, 4H), 1.24 (s, 1.5H), 1.17 (s, 1.5H). $^{13}C\{^{1}H\}$NMR (75.48 MHz, $CDCl_3$, δ): 175.1, 174.9, 137.3, 137.1, 129.3, 128.89, 128.86, 127.2, 114.4, 113.4, 108.6, 107.4, 68.2, 68.1, 52.2, 51.2, 30.6, 30.5, 29.8, 29.7, 23.8, 23.7, 19.2, 18.7. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{15}H_{18}NaO_6]^+$: 317.0996. Found: 317.0998. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.17. Found: C, 61.31; H, 6.23. IR (thin layer): 2986, 2895, 1801, 1497, 1456, 1380, 1234, 1175, 1079, 933, 845, 752, 701, 590 cm^{-1}.

Synthesis of peroxide 12 by reaction of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one (6q) with *t*-BuOH.

H_2SO_4 (98.0 mg, 1.00 mmol, 1.0 equiv.) and *t*-BuOH (74.0 mg, 1.00 mmol, 1.0 equiv.) were added with stirring to a solution of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one **6q** (224.21 mg, 1.00 mmol, 1.0 equiv.) in CH_2Cl_2 (2 mL). The reaction mixture was stirred at 20-25 °C for 4 days. Later, CH_2Cl_2 (50 mL) was added and the organic layer was washed with H_2O (3 × 10 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **12** was isolated by chromatography on SiO_2 (PE-EtOAc = 20:1).

4-Benzyl-5-(*tert*-butylperoxy)-5-methyl-1,2-dioxolan-3-one, 12

Yield 81% (227.1 mg, 0.81 mmol). Colorless oil. R_f = 0.27 (PE:EtOAc =20:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.38 – 7.24 (m, 5H), 3.30 – 3.20 (m, 2H), 3.08 (dd, *J* = 15.0, 11.1 Hz, 1H), 1.32 (s, 9H), 1.19 (s, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 175.5, 137.5, 129.2, 128.9, 127.1, 112.7, 82.2, 51.8, 30.9, 26.5, 18.9. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{15}H_{20}NaO_5]^+$: 303.1203. Found: 303.1199. Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H: 7.19. Found: C, 64.26; H, 7.15. IR (thin layer): 3031, 2983, 2935, 1801, 1604, 1498, 1456, 1366, 1263, 1192, 1176, 1085, 921, 853, 748, 700, 589 cm^{-1}.

Experimental Procedures for Scheme 7.

Procedure for the synthesis of 4-benzyl-5-hydroxy-5-methyl-1,2-dioxolan-3-one, 13

Ph_3P (288.5 mg, 1.10 mmol, 1.1 equiv.) in CH_2Cl_2 (2 mL) was added dropwise with stirring to a solution of **6q** (224.2 mg, 1.00 mmol, 1.0 equiv.) in CH_2Cl_2 (2 mL) at 0-10 °C. The reaction mixture was stirred at 20-25 °C for 1h and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Product **13** was isolated by chromatography on SiO_2 with elution using PE-EtOAc mixture (5:1).

4-Benzyl-5-hydroxy-5-methyl-1,2-dioxolan-3-one, 13

Yield 62% (129.0 mg, 0.62 mmol). White crystals, mp = 95-96 °C. R_f = 0.49 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 7.37 – 7.22 (m, 5H), 3.28 – 3.17 (m, 3H), 3.00 (dd, *J* = 14.8, 11.6 Hz, 1H), 1.20 (s, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 175.9, 137.2, 129.2, 128.9, 127.2, 108.2, 53.1, 31.0, 23.0. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{11}H_{12}NaO_4]^+$: 231.0628. Found: 231.0621. Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.51; H, 5.68. IR (KBr): 3651, 3425, 1764, 1458, 1399, 1268, 1228, 1194, 1075, 937, 757, 701, 608, 580 cm^{-1}.

Procedure for the synthesis of bisperoxide, 14 (procedure from Table 1, entry 2)

An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) was added with stirring to **1q** (220.3 mg, 1.00 mmol, 1.0 equiv.). Later, $BF_3{\cdot}Et_2O$ (709.5 mg, 5.00 mmol, 5.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Products **6q** (37%) and **14** (32%) were isolated by chromatography on SiO_2 with elution using PE-EtOAc mixture (5:1).

Ethyl 2-benzyl-3,3-dihydroperoxybutanoate, **14**

Yield 32% (86.5 mg, 0.32 mmol). Colorless oil. R_f = 0.22 (PE:EtOAc =5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$, δ): 9.43 (s, 1H), 9.20 (s, 1H), 7.32 – 7.16 (m, 5H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.51 (dd, *J* = 9.5, 5.6 Hz, 1H), 3.06 – 2.96 (m, 2H), 1.57 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$NMR (75.48 MHz, $CDCl_3$, δ): 172.1, 138.5, 129.0, 128.6, 126.8, 111.6, 61.7, 50.8, 33.8, 15.8, 14.0. HRMS (ESI-TOF) m/z $[M+Na]^+$. Calcd for $[C_{13}H_{18}NaO_6]^+$: 293.0996. Found: 293.0999. Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.61; H, 6.52. IR (film): 3320, 1800, 1715, 1455, 1377, 1219, 1084, 841, 750, 702 cm^{-1}.

Treatment of 4-benzyl-5-hydroxy-5-methyl-1,2-dioxolan-3-one, 13 by hydrogen peroxide.

An ethereal solution of H_2O_2 (2.048 M, 4.882 mL, 10.00 mmol, 10.0 equiv.) was added with stirring to **13** (208.2 mg, 1.00 mmol, 1.0 equiv.). Later, $BF_3 \cdot Et_2O$ (1.419 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Compound **13** (197.8 mg, 0.95 mmol) was recovered (95%) by chromatography on SiO_2 with elution using PE-EtOAc mixture (5:1).

Treatment of 4-benzyl-5-hydroperoxy-5-methyl-1,2-dioxolan-3-one, 6q by water.

H_2O (180.0 mg, 10.00 mmol, 10.0 equiv.) was added with stirring to **6q** (224.2 mg, 1.00 mmol, 1.0 equiv.) in Et_2O (5 mL). Later, $BF_3 \cdot Et_2O$ (1.419 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to the solution at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Compound **6q** (217.4 mg, 0.97 mmol) was recovered (97%) by chromatography on SiO_2 with elution using PE-EtOAc mixture (5:1).

Synthesis of 6q by $BF_3 \cdot Et_2O$-catalyzed cyclization of ethyl 2-benzyl-3,3-dihydroperoxybutanoate (14).

$BF_3 \cdot Et_2O$ (1.419 g, 10.00 mmol, 10.0 equiv.) was added dropwise with stirring to a solution **14** (270.3 mg, 1.00 mmol, 1.0 equiv.) in Et_2O (5 mL) at 0°C. The reaction mixture was stirred at 20-25 °C for 12 h. After that time, CH_2Cl_2 (40 mL) and H_2O (0.5 mL) were added. Then $NaHCO_3$ was added with stirring until pH reached 7.0. The precipitate was filtered off. The filtrate was dried over $MgSO_4$, filtered and concentrated under reduced pressure using a rotary evaporator (15-20 mmHg), (bath temperature, ca. 20–25 °C). Compound **6q** (215.2 mg, 0.96 mmol) was isolated by chromatography on SiO_2 with elution using PE-EtOAc mixture (5:1).

SUPPORTING INFORMATION

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Supplementary data about computational analysis, evaluation of oxidative properties of the β-hydroperoxy-β-peroxylactones with cyclic voltammetry, X-ray diffraction data, ^{1}H and ^{13}C NMR spectra, HRMS and IR spectra of all synthesized compounds (PDF).

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