JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Selective Synthesis of Cyclic Peroxides from Triketones and H_2O_2

Alexander O. Terent'ev,*[,†] Ivan A. Yaremenko,[†] Vladimir V. Chernyshev,[‡,§] Valery M. Dembitsky,[⊥] and Gennady I. Nikishin[†]

[†]N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation

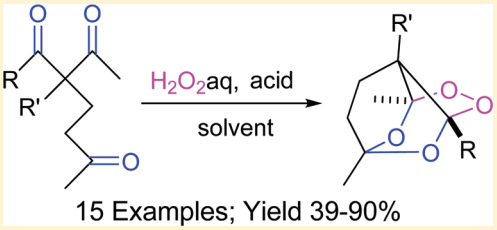
[‡]Department of Chemistry, Moscow State University, 119992 Moscow, Russian Federation

[§]A. N. Frumkin Institute of Physical Chemistry and Electrochemistry, 31 Leninsky prosp., 119991 Moscow, Russian Federation

[⊥]Institute for Drug Research, P.O. Box 12065, Hebrew University, Jerusalem 91120, Israel

Supporting Information

ABSTRACT: A method for the assembly of tricyclic structures containing the peroxide, monoperoxyacetal, and acetal moieties was developed based on the acid-catalyzed reaction of β,δ-triketones with H_2O_2. Tricyclic compounds are formed selectively in yields from 39% to 90% by the reactions with the use of large amounts of strong acids, such as H_2SO_4, $HClO_4$, or HBF_4, which act both as the catalyst and as the co-solvent. The reaction is unusual in that, despite the diversity of possible peroxidation pathways giving cyclic compounds and oligomers, the reaction proceeds with high selectivity and produces tricyclic peroxides via the monoperoxidation of the carbonyl groups in the β-positions and the transformation of the δ-carbonyl group into the acetal one. The syntheses are scaled up to tens of grams, and the resulting peroxides can be easily isolated from the reaction mixture.



INTRODUCTION

The history of the chemistry of organic peroxides dates back more than a century. During this period of time, ketones and aldehydes have been recognized as the key reagents in the synthesis of peroxides due to their availability and the ease of the reaction of the carbonyl carbon atom with the highly nucleophilic oxygen atom of the hydroperoxide group. Peroxides prepared from ketones are produced on a multiton scale and are widely used as initiators of the radical polymerization of unsaturated monomers.[1] In the past decades, the chemistry of organic peroxides has attracted considerable attention from physicians and pharmacologists because these compounds were found to have antimalarial,[2] antihelmintic,[3] and antitumor activities.[4] The interest in the synthesis of radical polymerization initiators and drugs gave impetus to the development of methods for the synthesis of peroxides with the use of carbonyl compounds, their derivatives, and H_2O_2 as the starting reagents.

The number of publications on the synthesis of peroxides by the reactions of H_2O_2 with monoketones runs into the hundreds,[5] the corresponding reactions with diketones were considered in about 10 publications,[6] and only one example of the synthesis with the use of triketones is known. Thus, a tricyclic compound containing three peroxide groups was synthesized in 18% yield from 3-acetylpentane-2,4-dione.[7] There is an opinion that the number of reaction products sharply increases with increasing number of carbonyl groups. Hence, the selective synthesis of peroxides based on triketones was regarded as an inherently difficult problem.

In the present study, we show that the reactions of triketones with H_2O_2 in the presence of acid catalysts result in the selective assembly of tricyclic structures, peroxides, containing only one O−O unit despite the use of more than an equimolar amount of hydrogen peroxide. The resulting tricyclic compounds are unusual in that they contain one acetal and two monoperoxyacetal moieties, which are as a rule unstable and can undergo peroxidation in the presence of water and hydrogen peroxide under acidic conditions,[8] and acetals are susceptible to hydrolysis.[9] The largest cycle in the tricyclic structure is seven-membered 1,2,4,6-tetroxepane. Peroxides on its base were prepared by ozonolysis of unsaturated compounds and cyclocondensation of intermediate products with aldehydes.[10]

RESULTS AND DISCUSSION

The peroxidation of β,δ-triketones **1a**−**o** with H_2O_2 in the presence of acids selectively produces tricyclic compounds **2a**−**o** containing one peroxide group (Scheme 1).

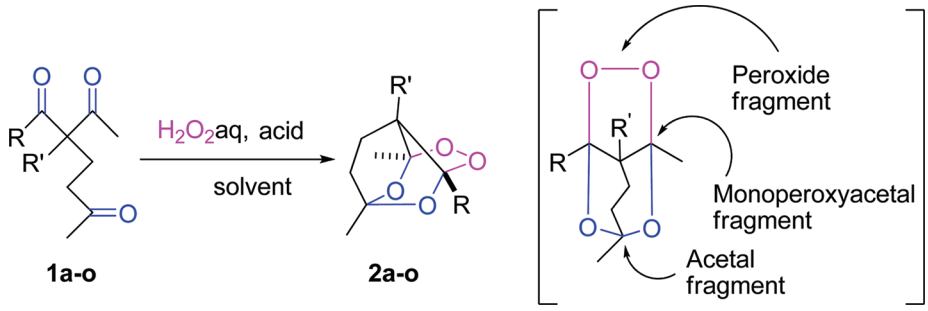
Strong protic acids H_2SO_4, $HClO_4$, and HBF_4 were used as the catalysts, which simultaneously acted as co-solvents.

The conditions of the preparation of tricyclic peroxides were optimized using the synthesis of 9-benzyl-1,4,6-trimethyl-2,3,5,10-tetraoxatricyclo[4.3.1.$0^{4,9}$]decane **2c** from 3-acetyl-3-benzylheptane-2,6-dione **1c** as an example. We examined the influence of the concentration and the nature of acid, the

Received: November 27, 2011
Published: January 17, 2012

 © 2012 American Chemical Society dx.doi.org/10.1021/jo202437r | J. Org. Chem. 2012, 77, 1833−1842

Scheme 1. Synthesis of Tricyclic Peroxides 2a–o from β,δ-Triketones 1a–o and H_2O_2



amount of hydrogen peroxide, and the synthesis procedure on the yield of tricyclic compound **2c** (Table 1).

Most experiments on the optimization were carried out in the presence of sulfuric acid as the catalyst using an aqueous solution of hydrogen peroxide in ethanol (runs 2–12); in the absence of the acid (run 1), the conversion of triketone **1c** was virtually absent. The highest yield of the target peroxide **2c** was achieved when using an equivalent amount and a 1.5-fold molar excess of H_2O_2 and a 8.7-fold molar excess of H_2SO_4 (81% and 74% in runs 4 and 7, respectively). It should be noted that the influence of the amount of sulfuric acid on the yield of **2c** passes through a maximum. Thus, at a small excess of the acid (runs 2 and 3), the reaction is not efficiently catalyzed (a complex mixture of peroxides is formed); at a large excess of the acid (run 6), the decomposition of peroxide occurs. Isopropanol (run 13), tetrahydrofuran (run 14), and acetonitrile (run 15) are less efficient solvents than ethanol.

As for other protic acids, tricyclic compound **2c** is produced in good yield only in the reactions catalyzed by HBF_4 and $HClO_4$ (runs 16 and 17; yields 56% and 65%, respectively). Weaker phosphoric acid is an inefficient catalyst for this reaction (run 18).

In the case of the aprotic acids I_2 (runs 19 and 20) and $SnCl_2{\cdot}2H_2O$ (runs 21 and 22), which are used for the peroxidation of carbonyl compounds,[11] tricyclic compound **2c** was obtained in low yield (lower than 22%) only in the reaction catalyzed by tin chloride.

The use of phosphomolybdic acid (runs 23–27), which proved to be a good catalyst for the preparation of, for example, vicinal hydroxyhydroperoxides,[12] geminal bishydroperoxides,[13] and tetraoxanes,[14] enables the synthesis of **2c** in good yield (65%, run 25), but the complete conversion of **1c** is not achieved.

Based on the results of the optimization, it can be concluded that a 1.5-fold molar excess of H_2O_2 and a 8–20-fold molar excess of the acid H_2SO_4, HBF_4, or $HClO_4$ are the key parameters determining good yields of tricyclic compound **2c**.

Taking into account these conditions, we synthesized a series of structurally related tricyclic compounds **2a,b,d–o** containing various functional groups and moieties: alkene **2e**, alkyne **2j**, nitrile **2i**, ester **2f**, nitro **2h**, and an aromatic core **2c**, **2g**, **2h**, and **2k–o** (Table 2).

As can be seen from Table 2, the above-described method is rather versatile and can be applied to the synthesis of tricyclic peroxides containing various functionalized substituents.

The fact that a large amount of acids facilitates the achievement of high yields of peroxides **2a–o** was unexpected. It is known that in an acidic medium peroxides tend to decompose, in particular, via the Baeyer–Villiger,[15] Criegee,[16] and Hock reactions.[17] The Hock and related decompositions may be expected in the case of peroxides **2k–o** containing the Ar-C-O-O moiety. However, under the above-described conditions, these reactions, if at all possible, do not influence significantly on the synthesis of tricyclic peroxides.

Apparently, the formation of tricyclic compounds **2** occurs via the peroxidation of one of the carbonyl groups in the β-positions. The intermediates containing the OOH group (which are susceptible to acid-catalyzed rearrangements due to a high O–O bond polarization) rapidly undergo cyclization to give dihydroxydioxolane followed by acetalyzation to form tricyclic compounds **2** whose weakly polarized O–O bond is less susceptible to acid-catalyzed transformations.

The reaction is unique in that, although it could give a diversity of peroxides as a result of the reaction of three carbonyl groups with binucleophilic H_2O_2, the product of monoperoxidation at the β-carbonyl groups is selectively formed. This result was unexpected considering that the formation of bridged tetraoxanes via the diperoxidation of β-carbonyl groups would be expected on the basis of the results of our earlier study on the peroxidation of β-diketones.[18]

Evidently, the presence of three carbonyl groups strictly in the β,δ-positions with respect to each other in molecule **1** determines the pathway of the peroxidation giving tricyclic peroxide **2**, which is not prone to undergo chemical transformations in the reaction medium. Under the optimal peroxidation conditions found for triketone **2c** (run 3, Table 1), the behavior of mono- and β-diketones differs from that of triketones **1**. We showed this fact with two examples (Scheme 2).

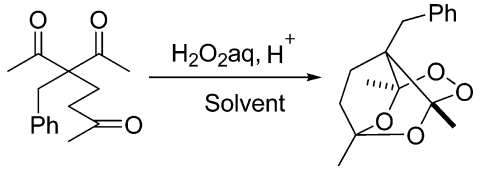
When performing the peroxidation of acetophenone **3**, we failed to achieve the complete conversion into geminal bishydroperoxide **4** because the reaction in an acidic aqueous medium is reversible.[19] In the case of benzoylacetone **5**, the complete conversion was observed, but the reaction gave a complex mixture of products. After the separation of resinous substances on SiO_2, the ^{13}C NMR spectrum showed signals characteristics of the carbonyl (δ 198), carboxy (δ 171–173), and O–C–O (δ 105–110) groups.

Therefore, the introduction of the third carbonyl group into the diketone molecule, i.e., in the case under consideration using 3-benzoylheptane-2,6-dione (**1k**) instead of benzoylacetone, provides the selectivity of the peroxidation and stability of the resulting peroxide **2k.**

Reactions of Tricyclic Peroxides 2c,e,f. To assess the resistance of tricyclic peroxides to reagents used in organic synthesis and to determine the structures, which are interesting to test for biological activity, we performed the halogenation, oxidation, alkaline hydrolysis, amidation, and reduction (Scheme 3).

dx.doi.org/10.1021/jo202437r | J. Org. Chem. 2012, 77, 1833–1842

Table 1. Results of the Optimization of the Conditions for the Synthesis of 9-Benzyl-1,4,6-trimethyl-2,3,5,10-tetraoxatricyclo[4.3.1.0^{4,9}]decane 2c from 3-Acetyl-3-benzylheptane-2,6-dione 1c



1c **2c**

		acid				
run	mole H_2O_2 per mole **1c**	formula	mmole (mole per mole **1c**)	solvent (procedure)[a]	conv of **1c**, %	yield **2c**, % (based on NMR)
1	1.5			EtOH (A)	5	0
2	1.5	H_2SO_4	1 (0.9)	EtOH (A)	80	8
3	1.5	H_2SO_4	5 (4.4)	EtOH (A)	95	31
4	1.5	H_2SO_4	10 (8.7)	EtOH (A)	100	81, 73[b]
5	1.5	H_2SO_4	20 (17.4)	EtOH (A)	100	47, 40[b]
6	1.5	H_2SO_4	50 (43.5)	EtOH (A)	100	35
7	1	H_2SO_4	10 (8.7)	EtOH (A)	90	74, 62[b]
8	1	H_2SO_4	10 (8.7)	EtOH (A)[c]	95	58
9	1	H_2SO_4	10 (8.7)	EtOH (A)[d]	95	42
10	2	H_2SO_4	10 (8.7)	EtOH (A)	100	50
11	3	H_2SO_4	10 (8.7)	EtOH (A)	100	44
12	7	H_2SO_4	10 (8.7)	EtOH (A)	100	42, 34[b]
13	1.5	H_2SO_4	10 (8.7)	*i*-PrOH (A)	95	52
14	1.5	H_2SO_4	10 (8.7)	THF (A)	100	67, 60[b]
15	1.5	H_2SO_4	10 (8.7)	CH_3CN (A)	100	48
16	1.5	HBF_4	20 (17.4)	EtOH (B)	100	56
17	1.5	$HClO_4$	20 (17.4)	EtOH (B)	100	65, 58[b]
18	1.5	H_3PO_4	6 (5.2)	EtOH (B)	20	traces
19	4.0	I_2	0.12 (0.1)	CH_3CN (C)	10	0
20	1.5	I_2	0.58 (0.5)	CH_3CN (C)	90	0
21	1.5	$SnCl_2{\cdot}2H_2O$	0.12 (0.1)	CH_3CN (D)	43	13
22	1.5	$SnCl_2{\cdot}2H_2O$	0.58 (0.5)	CH_3CN (D)	60	22
23	1.5	PMA	0.43 (0.37)	EtOH (E)	16	13
24	1.5	PMA	0.09 (0.074)	Et_2O (E)	50	42
25	1.5	PMA	0.43 (0.37)	Et_2O (E)	80	65, 57[b]
26	1.5	PMA	0.85 (0.74)	Et_2O (E)	80	61
27	1.5	PMA	1.71 (1.49)	Et_2O (E)	80	41, 35[b]

[a]General procedures A–E for the synthesis: (A) A 37% aqueous H_2O_2 solution (0.106–0.740 g, 1.15–8.05 mmol) and a solution of H_2SO_4 (0.10–5.0 g, 1–50 mmol) (in run 1, in the absence of H_2SO_4) in EtOH (*i*-PrOH, THF, or CH_3CN; 1 mL) were added with stirring to a solution of triketone **1c** (0.30 g, 1.15 mmol) in EtOH (*i*-PrOH, THF, or CH_3CN; 4 mL) at 10–15 °C. The reaction mixture was stirred at 20–25 °C for 1 (3 or 20) h. (B) A 37% aqueous H_2O_2 solution (0.159 g, 1.73 mmol) and a solution of HBF_4, $HClO_4$, or H_3PO_4 (0.692–3.51 g, 6–20 mmol) in EtOH (1 mL) were added with stirring to a solution of triketone **1c** (0.30 g, 1.15 mmol) in EtOH (4 mL) at 10–15 °C. The reaction mixture was stirred at 20–25 °C for 1 h. (C) Triketone **1c** (0.30 g, 1.15 mmol) was added to a solution of I_2 (0.03 or 0.147 g, 0.12 or 0.58 mmol) and a 37% aqueous H_2O_2 solution (0.423 or 0.159 g, 4.6 or 1.73 mmol of H_2O_2) in CH_3CN (10 mL). The reaction mixture was stirred at 20–25 °C for 24 h. (D) A mixture of triketone **1c** (0.30 g, 1.15 mmol), a 37% aqueous H_2O_2 solution (0.159 g, 1.73 mmol of H_2O_2), and $SnCl_2{\cdot}2H_2O$ (0.027 or 0.131 g, 0.12 and 0.58 mmol) in MeCN (5 mL) was stirred at 20–25 °C for 24 h. (E) A 37% aqueous H_2O_2 solution (0.159 g, 1.73 mmol) and phosphomolybdic acid (PMA) (0.20–4.0 g, 0.09–1.71 mmol) were successively added with stirring to a solution of triketone 1c (0.30 g, 1.15 mmol) in Et_2O or EtOH (10 mL) at room temperature. The reaction mixture was stirred at 20–25 °C for 24 h. [b]Yield based on the isolated product. [c]Reaction time was 3 h. [d]Reaction time was 20 h.

The tricyclic peroxide moiety is resistant to *m*-chloroperbenzoic acid, alkalies, ethyl chloroformate, and amines, which enabled us to synthesize epoxide **6**, acid **7**, and amides **8** and **9** in high yields (76–95%). The course of the reaction of **2c** with triphenylphosphine was monitored by NMR spectroscopy. The spectrum showed only signals of triketone **1c**, which was isolated in quantitative yield. The cyclic product of the insertion of the phosphorus atom at the O–O bond, whose analogues were observed, for example, in the studies,[20] was not detected by ^{31}P NMR spectroscopy.

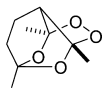
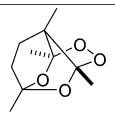
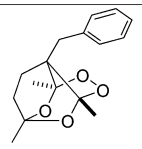
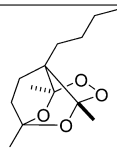
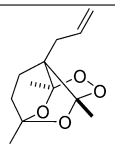
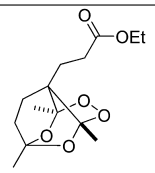
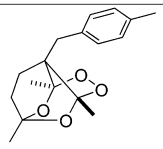
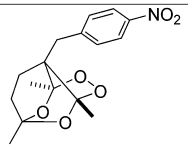
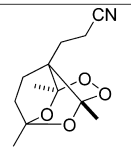
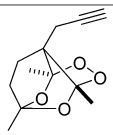
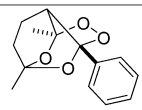
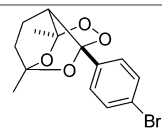
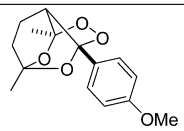
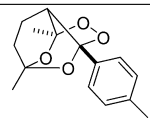
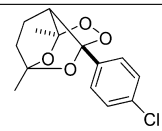
The bromination of tricyclic peroxide **2e** gave a complex mixture of reaction products.

The resistance of tricyclic structures to heating was studied using peroxide **2c** as an example (see the Experimental Section). Virtually no decomposition of the peroxide was observed during refluxing for 1 h in EtOH. In the presence of H_2SO_4, the peroxide was completely decomposed after refluxing in EtOH to form a complex mixture of reaction products.

Establishment of the Structures of Tricyclic Peroxides 2a–o and 6–9. All peroxides **2a–o** and **6–9** are solids with melting points from 43–44 °C (**2e**) to 159–160 °C (**6**). Their structures were established by ^1H and ^{13}C NMR spectroscopy, ESI-HRMS mass spectrometry, and elemental analysis. In the

dx.doi.org/10.1021/jo202437r | J. Org. Chem. 2012, 77, 1833–1842

Table 2. Structures and Yields of Tricyclic Peroxides 2a–o[a]

Structure, yield %[b]		
 **2a,** 58	 **2b,** 61	 **2c,** 70
 **2d,** 84	 **2e,** 63 (71)[c]	 **2f,** 54 (65)[c]
 **2g,** 52[d]	 **2h,** 61[e]	 **2i,** 82
 **2j,** 82	 **2k,** 73	 **2l,** 84
 **2m,** 39	 **2n,** 90	 **2o,** 78

[a]**General procedure:** a 37% aqueous H_2O_2 solution (1.5 mol of H_2O_2 per mole of triketone **1a–o**) and a solution of H_2SO_4 (1 g) in EtOH (1 mL) were successively added to a solution of triketone **1a–o** (0.30 g) in EtOH (4 mL) at 10–15 °C. The reaction mixture was stirred at 20–25 °C for 1 h. [b]Yield based on the isolated product. [c]Experiments were scaled up to 10 times larger initial amounts of the reagents. [d]Reaction time was 2 h. [e]Because of the low solubility of **1h**, a mixture of THF (3 mL) and EtOH (2 mL) was used as the solvent.

^{13}C NMR spectra, the most informative signals are those for the carbon atoms of the monoperoxyacetal OOCO (δ 104.8–107.5) and acetal OCO (δ 93.7–95.9) moieties, whose chemical shifts are similar to those of known monoperoxyacetals[21] and acetals.[22]

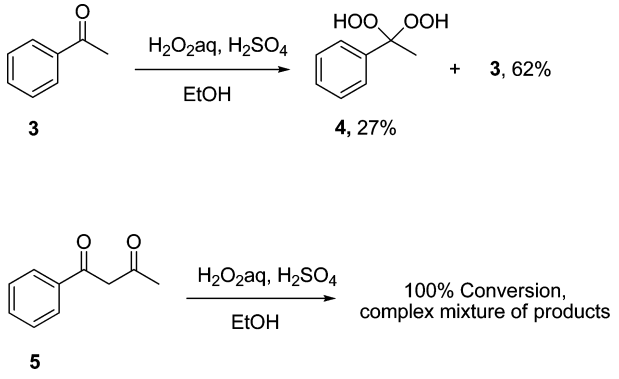
Despite the NMR spectroscopic data, the establishment of the structures of organic peroxides is always a difficult problem because of the possible formation of peroxide oligomers or rearrangements accompanied by changes in the carbon skeleton and the formation of the ester group. Hence, compounds **2b** and **2l** were studied by X-ray diffraction, which confirmed their structures (see the Supporting Information).

■ CONCLUSION

A selective method for the synthesis of the previously unknown peroxide structures was developed based on the acid-catalyzed reaction of β,δ-triketones with H_2O_2. The process is unusual in that, despite the diversity of possible pathways in the presence of a large excess of strong acids (H_2SO_4, $HClO_4$, or HBF_4) as the catalyst, the reaction of β,δ-triketones with hydrogen peroxide follows one pathway and produces tricyclic com-

dx.doi.org/10.1021/jo202437r | J. Org. Chem. 2012, 77, 1833–1842

Scheme 2. Acid-Catalyzed Reactions of Acetophenone 3 and Benzoylacetone 5 with H_2O_2



pounds via the monoperoxidation of the carbonyl groups in the β-positions and the transformation of the δ-carbonyl group into the acetal one. Apparently, due to the geometry of tricyclic compounds, the monoperoxyacetal and acetal moieties are stable even despite the presence of water, ethanol, and hydrogen peroxide in the reaction mixture. Unlike many compounds containing the O−O bond, which are rearranged in acidic media, the resulting cyclic peroxides are quite stable under the reaction conditions.

The tricyclic compounds are produced in 39−90% yields and can be easily isolated from the reaction mixture. The reaction is scaled up to several grams.

EXPERIMENTAL SECTION

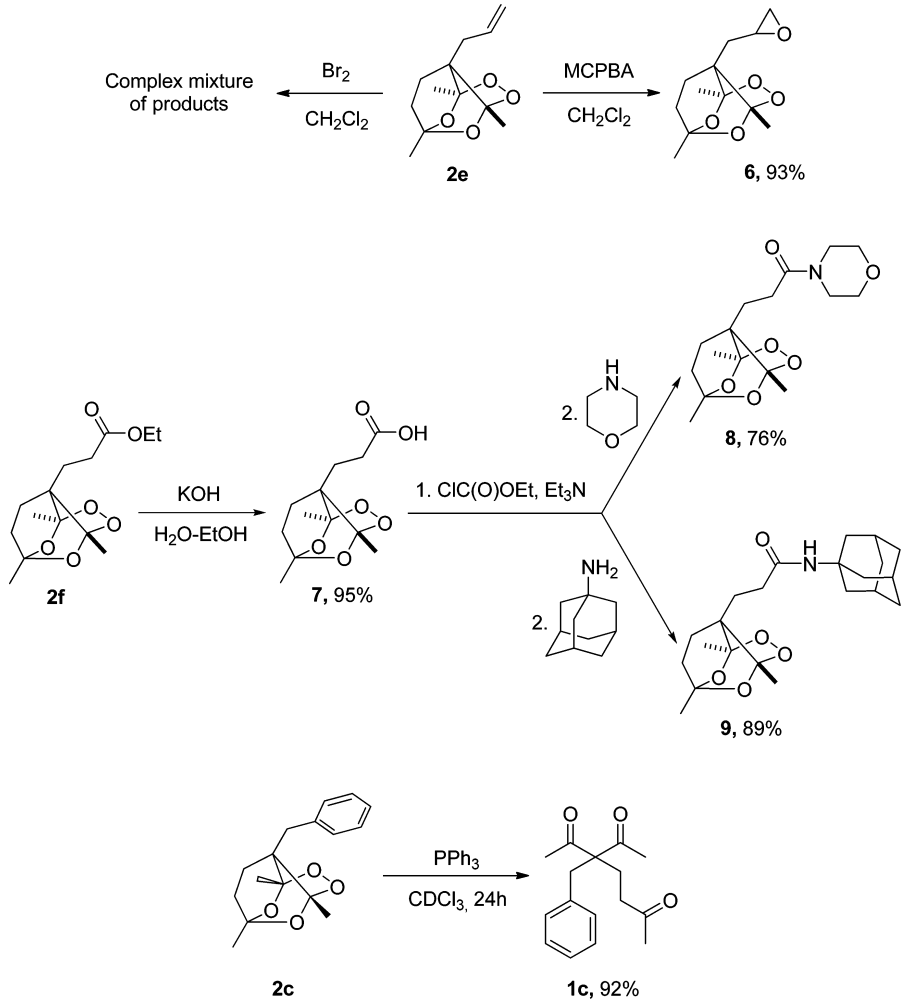
Caution: Although we have encountered no difficulties in working with peroxides, precautions such as the use of shields, fume hoods, and the avoidance of transition metal salts, heating and shaking should be taken whenever possible.

NMR spectra were recorded on a commercial instrument (300.13 MHz for ^{1}H, 75.48 MHz for ^{13}C) in $CDCl_3$. High-resolution mass spectra (HRMS) were measured in the electrospray ionization (ESI) mode[23] The measurements were taken in the positive ion mode (the interface capillary voltage was 4500 V); the mass range was from m/z 50 to m/z 3000 Da; the external/internal calibration was done with Electrospray Calibrant Solution. The syringe injection was used for solutions in acetonitrile (flow rate was 3 μL/min). Nitrogen was used as a dry gas; the 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 hot-stage apparatus. Chromatography was performed on silica gel (63−200 mesh).

Acetone, EtOH, *i*-PrOH, CH_2Cl_2, Et_2O, petroleum ether (PE) (40/70), CH_3CN, THF, ethyl acetate (EA), $HClO_4$ (60% aqueous solution), HBF_4 (50% aqueous solution), H_3PO_4 (85% aqueous solution), H_2SO_4, phosphomolybdic acid hydrate (ca. 78% phosphomolybdic acid, PMA), 3-chloroperoxybenzoic acid (MCPBA, 70−75%

Scheme 3. Reactions of Tricyclic Peroxides 2c,e,f



dx.doi.org/10.1021/jo202437r | J. Org. Chem. 2012, 77, 1833−1842

balance 3-chlorobenzoic acid and water), morpholine, Et_3N, 1-adamantanamine hydrochloride, acetylacetone, acetophenones, methyl vinyl ketone, benzyl and alkyl bromides, allyl bromide, propargyl bromide, ethyl acrylate, acrylonitrile, ethyl chloroformate, 1-phenylbutane-1,3-dione, Ph_3P, H_2O_2 (37% aqueous solution), benzyltriethylammonium chloride (98%), Na_2SO_4, K_2CO_3, $NaHCO_3$, NaOH, KOH, I_2, $FeCl_3{\cdot}6H_2O$, $SnCl_2{\cdot}2H_2O$, NaI, and $CeCl_3{\cdot}7H_2O$ were commercial products and were used as is.

Synthesis of β,δ-Triketones 1a−o. β,δ-Triketones **1a** and **1b** were synthesized according to a known procedure.[24]

3-Acetylheptane-2,6-dione, 1a.[24] Colorless oil. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.97−2.16 (m, 11H), 2.40 (t, 2H, *J* = 7.0 Hz), 3.63 (t, 0.8H, *J* = 7.0 Hz), 16.64 (br.s, 0.2H).

3-Acetyl-3-methylheptane-2,6-dione, 1b.[24] Colorless oil. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.30 (s, 3H), 1.99−2.16 (m, 11H), 2.31 (t, 2H, *J* = 7.7 Hz).

Triketone **1c** was synthesized according to a published procedure.[24] Methyl vinyl ketone (4.91 g, 70 mmol) was added dropwise with stirring to a solution of $FeCl_3{\cdot}6H_2O$ (0.865 g, 3.2 mmol) in 3-benzylpentane-2,4-dione (12.00 g, 63 mmol) at 20−25 °C. The mixture was stirred at 20−25 °C until it completely solidified, and the solid was dissolved in CH_2Cl_2 (50 mL). The organic layer was washed with a saturated $NaHCO_3$ solution (4 × 10 mL), a 5% aqueous HCl solution until the organic phase became colorless, and water (2 × 15 mL), dried over Na_2SO_4, and filtered. The solvent was removed in a water jet vacuum. Triketone **1c** was recrystallized from *i*-PrOH. Compound **1c** (10.93 g, 42 mmol), yield 67%.

3-Acetyl-3-benzylheptane-2,6-dione, 1c. White crystals. Mp = 79−80 °C. R_f = 0.34 (TLC, PE/EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.09 (s, 11H), 2.26−2.34 (m, 2H), 3.16 (s, 2H), 6.97−7.06 (m, 2H), 7.16−7.27 (m, 3H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 24.2, 27.7, 29.9, 37.5, 38.0, 70.0, 127.0, 128.5, 129.6, 135.5, 206.8, 206.9. Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.79; H, 7.88.

Triketones **1d−j** were synthesized according to a known procedure.[25] Methyl vinyl ketone (0.328−0.558 g, 4.68−7.96 mmol), $CeCl_3{\cdot}7H_2O$ (0.317−0.540 g, 0.85−1.45 mmol), and NaI (0.064−0.109 g, 0.43−0.73 mmol) were successively added with stirring to a solution of the corresponding β-diketone (1.00 g, 4.25−7.24 mmol) in MeCN (1 mL) at 20−25 °C. The reaction mixture was stirred at room temperature for 12 h. Then CH_2Cl_2 (20 mL) was added, the catalyst was filtered off, and the precipitate was washed on the filter with CH_2Cl_2 (20 mL). The solvents were removed in a water jet vacuum. Products **1d−j** were isolated by chromatography on SiO_2 using a PE/EA mixture as the eluent with a gradient of ethyl acetate from 40 to 90 vol %. Compounds **1d** (1.01 g, 4.48 mmol), yield 70%; **1e** (1.26 g, 5.99 mmol), yield 84%; **1f** (1.05 g, 3.90 mmol), yield 78%; **1g** (0.765 g, 2.79 mmol), yield 57%; **1h** (1.08 g, 3.53 mmol), yield 83%; **1i** (0.947 g, 4.24 mmol), yield 65%; **1j** (1.24 g, 5.93 mol), yield 82%.

3-Acetyl-3-butylheptane-2,6-dione, 1d. White crystals. Mp = 45−46 °C. R_f = 0.51 (TLC, PE/EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 0.85 (t, 3H, *J* = 7.0 Hz), 0.92−1.05 (m, 2H), 1.21−1.34 (m, 2H), 1.75−1.84 (m, 4H), 2.01−2.12 (m, 9H), 2.15−2.24 (m, 2H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 13.7, 23,1, 24,2, 25.9, 26.9, 29.9, 31.4, 38.1, 69.3, 207.2. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.28; H, 10.09.

3-Acetyl-3-allylheptane-2,6-dione, 1e. Yellow oil. R_f = 0.51 (TLC, PE/EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.94−2.30 (m, 13H), 2.57 (d, 2H, *J* = 7.3 Hz), 4.98−5.15 (m, 2H), 5.38−5.56 (m, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 24.3, 27.1, 29.9, 35.9, 37.7, 69.1, 119.2, 131.6, 206.3, 207.0. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.54; H, 8.99.

Ethyl 4,4-Diacetyl-7-oxooctanoate, 1f. Colorless oil. R_f = 0.37 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.20 (t, 3H, *J* = 7.0 Hz), 2.00−2.30 (m, 17H), 4.08 (q, 2H, *J* = 7.0 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 14.1, 24.1, 26.1, 26.9, 28.8, 29.9, 37.7, 60.7, 68.4, 172.4, 206.5, 206.8. Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 62.44; H, 8.38.

3-Acetyl-3-(4-methylbenzyl)heptane-2,6-dione, 1g. White crystals. Mp = 125−126 °C. R_f = 0.56 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.09 (s, 11H), 2.24−2.35 (m, 5H), 3.12 (s, 2H), 6.87 (d, 2H, *J* = 7.3 Hz), 7.03 (d, 2H, *J* = 7.3 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 20.9, 24.2, 27.8, 30.0, 37.1, 38.0, 70.1, 129.2, 129.4, 132.2, 136.7, 206.9, 207.1. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.46; H, 8.09.

3-Acetyl-3-(4-nitrobenzyl)heptane-2,6-dione, 1h. Hazel crystals. Mp = 113−114 °C. R_f = 0.31 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.11 (s, 11H), 2.32 (t, 2H, *J* = 7.7 Hz), 3.24 (s, 2H), 7.19 (d, 2H, *J* = 8.8 Hz), 8.08 (d, 2H, *J* = 8.8 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 24.5, 27.8, 30.0, 37.1, 37.7, 70.0, 123.6, 130.6, 143.6, 147.1, 206.1, 206.3. Anal. Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.74; H, 6.37; N, 4.59.

4,4-Diacetyl-7-oxooctanenitrile, 1i. Hazel crystals. Mp = 74−75 °C. R_f = 0.27 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.05−2.31 (m). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 12.5, 24.1, 26.8, 26.9, 30.0, 37.4, 68.3, 118.7, 205.6, 206.1. Anal. Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.80; H, 8.00; N, 6.21.

3-Acetyl-3-(2-propynyl)-2,6-heptanedione, 1j. Yellow crystals. Mp = 54−55 °C. R_f = 0.55 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.02 (t, 1H, *J* = 2.7 Hz), 2.09−2.16 (m, 9H), 2.25−2.32 (m, 4H), 2.70 (d, 2H, *J* = 2.7 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 21.3, 24.6, 26.9, 29.9, 37.8, 68.5, 72.2, 78.8, 204.9, 206.7. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.11; H, 7.83.

Triketones **1k−o** were synthesized according to a known procedure.[26] Methyl vinyl ketone (1.45−2.16 g, 20.75−30.85 mmol) was added with stirring to a solution of the corresponding β-diketone (1.00 g, 4.15−6.17 mmol) in EtOH (10 mL). The mixture was refluxed for 24 h and then cooled. Ethanol and methyl vinyl ketone that remained unconsumed were removed in a water jet vacuum. Products **1k−o** were isolated by chromatography on SiO_2 using a PE/EA mixture as the eluent with a gradient of ethyl acetate from 30 to 90 vol %. Products **1k** (1.22 g, 5.24 mmol), yield 85%; **1l** (0.697 g, 2.24 mmol), yield 54%; **1m** (1.01 g, 3.85 mmol), yield 74%; **1n** (0.628 g, 2.55 mmol), yield 45%; **1o** (0.707 g, 2.65 mmol), yield 52%.

3-Benzoylheptane-2,6-dione, 1k.[26] Yellow oil. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.95−2.28 (m, 8H), 2.35−2.61 (m, 2H), 4.53 (t, H, *J* = 6.6 Hz), 7.39−7.60 (m, 3H), 7.98 (d, 2H, *J* = 8.1 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 22.4, 28.5, 29.9, 40.4, 61.0, 128.6, 128.8, 133.8, 136.1, 196.5, 203.9, 207.8.

3-(4-Bromobenzoyl)heptane-2,6-dione, 1l. White crystals. Mp = 70−71 °C. R_f = 0.45 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.03−2.21 (m, 8H), 2.39−2.61 (m, 2H), 4.48 (t, H, *J* = 6.6 Hz), 7.61 (d, 2H, *J* = 8.1 Hz), 7.87 (d, 2H, *J* = 8.1 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 22.3, 28.5, 29.9, 40.3, 61.1, 129.2, 130.2, 132.2, 134.8, 195.6, 203.7, 207.8. Anal. Calcd for $C_{14}H_{15}BrO_3$: C, 54.04; H, 4.86; Br, 25.68. Found: C, 54.07; H, 5.01; Br, 25.62.

3-(4-Methoxybenzoyl)heptane-2,6-dione, 1m. Brown oil. R_f = 0.33 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.01−2.23 (m, 8H), 2.35−2.60 (m, 2H), 3.83 (s, 3H), 4.46 (t, H, *J* = 7.0 Hz), 6.92 (d, 2H, *J* = 8.8 Hz), 7.98 (d, 2H, *J* = 8.8 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 22.5, 28.3, 29.9, 40.5, 55.5, 60.8, 114.0, 129.1, 131.1, 164.1, 194.8, 204.2, 207.9. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.43; H, 7.25.

3-(4-Methylbenzoyl)heptane-2,6-dione, 1n. Colorless oil. R_f = 0.56 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.05−2.30 (m, 8H), 2.34−2.63 (m, 5H), 4.53 (t, 1H, *J* = 7.3 Hz), 7.29 (d, 2H, *J* = 8.3 Hz), 7.92 (d, 2H, *J* = 8.3 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 21.6, 22.4, 28.5, 29.9, 40.5, 61.0, 128.9, 129.6, 133.8, 144.9, 196.1, 204.1, 207.9. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.03; H, 7.40.

3-(4-Chlorobenzoyl)heptane-2,6-dione, 1o. White crystals. Mp = 56−57 °C. R_f = 0.56 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.03−2.23 (m, 8H), 2.39−2.61 (m, 2H), 4.49 (t, H, *J* = 6.6 Hz), 7.45 (d, 2H, *J* = 8.1 Hz), 7.96 (d, 2H, *J* = 8.1 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 22.4, 28.5, 30.0, 40.4, 61.2, 129.2, 130.2, 134.4, 140.5, 195.4, 203.7, 207.8. Anal. Calcd for $C_{14}H_{15}ClO_3$: C, 63.04; H, 5.67; Cl, 13.29. Found: C, 63.07; H, 5.72; Cl, 13.18.

Synthesis of 9-Benzyl-1,4,6-trimethyl-2,3,5,10-tetraoxatricyclo[4.3.1.0^{4,9}]decane 2c (Table 1, runs 1−27). General Procedure for Peroxidation of 1c without

(Table 1, experiment 1) and with the Use of H_2SO_4 (Table 1, runs 2−15). A 37% aqueous H_2O_2 solution (0.106−0.740 g, 1.15−8.05 mmol) and a solution of H_2SO_4 (0.1−5 g, 1−50 mmol) in EtOH (*i*-PrOH, THF, or CH_3CN; 1 mL) were added with stirring to a solution of triketone **1c** (0.30 g, 1.15 mmol) in EtOH (*i*-PrOH, THF, or CH_3CN; 4 mL) at 10−15 °C; in run 1, a solution of H_2SO_4 was not added. The reaction mixture was stirred at 20−25 °C for 1 h, and a mixture of CH_2Cl_2/PE = 1:1 (10 mL) was added. Then $NaHCO_3$ was added to the reaction mixture with stirring until the pH reached 7.0; in run 1, $NaHCO_3$ was not added. The precipitate was filtered off. The filtrate was dried over Na_2SO_4, the precipitate was filtered off, and the solvent was removed in a water jet vacuum. In runs 4, 5, 7, 12, and 14, product **2c** was isolated by chromatography on SiO_2 using a PE/EA mixture as the eluent with a gradient of ethyl acetate from 5 to 40 vol %.

General Procedure for Peroxidation of 1c with the Use of HBF_4 (50% aqueous solution), $HClO_4$ (60% aqueous solution), and H_3PO_4 (Table 1, runs 16−18). A 37% aqueous H_2O_2 solution (0.159 g, 1.73 mmol) and a solution of HBF_4, $HClO_4$, or H_3PO_4 (0.69−3.51 g, 6−20 mmol) in EtOH (1 mL) were added with stirring to a solution of triketone **1c** (0.30 g, 1.15 mmol) in EtOH (4 mL) at 10−15 °C. The reaction mixture was stirred at 20−25 °C for 1 h. Compound **2c** was isolated, and the yield was calculated as described in runs 1−15; in run 17, the yield was determined based on the isolated **2c**.

Procedure for Peroxidation of 1c with the Use of I_2 (Table 1, runs 19 and 20). Molecular iodine (0.03 or 0.147 g, 0.12 or 0.58 mmol) and a 37% aqueous H_2O_2 solution (0.423 or 0.159 g, 4.6 or 1.73 mmol) were dissolved in CH_3CN (10 mL), and then triketone **1c** (0.30 g, 1.15 mmol) was added to the solution. The reaction mixture was stirred at 20−25 °C for 24 h. Target peroxide **2c** was not detected by TLC in the course of the reaction and after the synthesis.

Procedure for Peroxidation of 1c with the Use of $SnCl_2{\cdot}2H_2O$ (Table 1, runs 21 and 22). A mixture of triketone **1c** (0.30 g, 1.15 mmol), a 37% aqueous H_2O_2 solution (0.159 g, 1.73 mmol), and $SnCl_2{\cdot}2H_2O$ (0.027 or 0.131 g, 0.12 and 0.58 mmol) in CH_3CN (5 mL) was stirred at 20−25 °C for 24 h. Then CH_2Cl_2 (40 mL) was added. The organic layer was washed with water (10 mL), a 5% aqueous $NaHCO_3$ solution (2 × 10 mL), and again with water (10 mL). The organic layer was dried over Na_2SO_4 and filtered. The solvent was removed in a water jet vacuum. Compound **2c** was isolated, and the yield was calculated as described in runs 1−15.

General Procedure for Peroxidation of 1c with the Use of PMA (Table 1, runs 23−27). A 37% aqueous H_2O_2 solution (0.159 g, 1.73 mmol) and phosphomolybdic acid (PMA) (0.20−4.0 g, 0.09−1.71 mmol) were successively added with stirring to a solution of triketone **1c** (0.30 g, 1.15 mmol) in Et_2O or EtOH (10 mL) at room temperature. The reaction mixture was stirred at 20−25 °C for 24 h, and then CH_2Cl_2 (30 mL) was added. The organic layer was washed with water (10 mL), a 5% aqueous $NaHCO_3$ solution (2 × 10 mL), and again with water (10 mL). The organic layer was dried over Na_2SO_4 and filtered. The solvent was removed in a water jet vacuum. Compound **2c** was isolated, and the yield was calculated as described in runs 1−15. In runs 25 and 27, the yield was determined based on the isolated **2c**.

In runs 1−27, the conversion of **1c** (the characteristic signal is a singlet of the CH_2C_{arom} group at δ 3.16) and the yield of **2c** (the characteristic signal is a singlet of the CH_2C_{arom} group at δ 2.86) were determined from the ^1H NMR spectroscopic data based on the starting triketone **1c**. 1,4-Dioxane was used as the internal standard (the characteristic signal is a singlet of the CH_2 group at δ 3.69).

General Procedure for the Synthesis of Tricyclic Peroxides 2a−o (Table 2). A 37% aqueous H_2O_2 solution (0.132−0.243 g, 1.44−2.64 mmol) and a solution of H_2SO_4 (1.0 g, 0.01 mol) in EtOH (1 mL; THF/EtOH = 3:2 in the case of triketone **1h**) were added with stirring to a solution of triketone **1a−o** (0.30 g, 0.96−1.76 mmol) in EtOH (4 mL; THF/EtOH = 3:2 in the case of triketone **1h**) at 10−15 °C. The reaction mixture was stirred at 20−25 °C for 1 h (in the case of triketone **1g**, for 2 h), and a mixture of CH_2Cl_2/PE = 1:1 (10 mL) was added. Then $NaHCO_3$ was added to the reaction mixture with stirring until the pH reached 7.0. The precipitate was filtered off. The filtrate was dried over Na_2SO_4, the precipitate was filtered off, and the solvent was removed in a water jet vacuum. Products **2a−o** were isolated by chromatography on SiO_2 using a PE/EA mixture as the eluent with a gradient of ethyl acetate from 5 to 50 vol %.

The scaled-up synthesis of **2e,f** with an increase in the amounts of the starting reagents and solvents by a factor of 10 was performed in the same way.

3,6,7a-Trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo-[3,4-*b*]pyran, 2a. White crystals. Mp = 73−74 °C. R_f = 0.24 (TLC, PE/EA, 5:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.52 (s, 6H), 1.60−1.70 (m, 2H), 1.79−1.91 (m, 2H), 2.30−2.38 (m, H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 13.1, 17.7, 24.6, 29.2, 47.8, 95.3, 104.8. Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.07; H, 7.62. HRMS (ESI): *m*/*z* $[M + NH_4]^+$ calcd for $[C_9H_{18}NO_4]^+$ 204.1230; found 204.1236.

3,3a,6,7a-Tetramethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran, 2b. White crystals. Mp = 94−95 °C. R_f = 0.49 (TLC, PE/EA, 5:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.0 (s, 3H), 1.39 (s, 3H), 1.43 (s, 6H), 1.64−1.73 (m, 4H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 15.3, 17.0, 21.2, 24.8, 31.2, 48.2, 94.3, 107.0. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.26; H, 8.26. HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $[C_{10}H_{16}NaO_4]^+$ 223.0941; found 223.0942.

3a-Benzyl-3,6,7a-trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran, 2c. White crystals. Mp = 94−95 °C. R_f = 0.37 (TLC, PE/EA, 5:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.42 (s, 6H), 1.65−1.74 (m, 2H), 1.79−1.88 (m, 2H), 2.86 (s, 2H), 7.15−7.32 (m, 5H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 16.1, 18.9, 24.7, 30.9, 36.8, 51.7, 93.7, 107.5, 126.8, 128.1, 131.2, 136.4. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.64; H, 7.25. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $[C_{16}H_{21}O_4]^+$ 277.1434; found 277.1433.

3a-Butyl-3,6,7a-trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran, 2d. White crystals. Mp = 60−61 °C. R_f = 0.39 (TLC, PE/EA, 5:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J* = 7.0 Hz), 1.20−1.52 (m, 15H), 1.67−1.71 (m, 4H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 13.8, 16.1, 18.9, 23.6, 24.8, 26.3, 30.87, 30.94, 50.6, 94.0, 107.3. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.33; H, 9.35. HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $[C_{13}H_{23}O_4]^+$ 243.1591; found 243.1591.

3a-Allyl-3,6,7a-trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran, 2e. White crystals. Mp = 43−44 °C. R_f = 0.45 (TLC, PE/EA, 5:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.47 (s, 6H), 1.70−1.72 (m, 4H), 2.27 (d, 2H, *J* = 7.3 Hz), 5.04−5.15 (m, 2H), 5−79−5.95 (m, H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 16.1, 19.0, 24.7, 30.8, 35.8, 50.7, 94.0, 107.1, 118.5, 133.2. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 64.02; H, 7.95. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $[C_{12}H_{19}O_4]^+$ 227.1279; found 227.1278.

Ethyl 3-(3,6,7a-Trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran-3a-yl)propanoate, 2f. White crystals. Mp = 57−58 °C. R_f = 0.45 (TLC, PE/EA, 2:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.23 (t, 3H, *J* = 7.1 Hz), 1.38 (s, 3H), 1.46 (s, 6H), 1.67−1.70 (m, 4H), 1.76−1.83 (m, 2H), 2.47−2.54 (m, 2H), 4.1 (q, 2H, *J* = 7.1 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 14.2, 15.7, 20.0, 24.6, 26.5, 29.4, 30.7, 50.2, 60.6, 94.1, 106.8, 173.3. Anal. Calcd $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found: C, 58.75; H, 7.81. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $[C_{14}H_{22}NaO_6]^+$ 309.1309; found 309.1307.

3,6,7a-Trimethyl-3a-(4-methylbenzyl)tetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran, 2g. White crystals. Mp = 104−105 °C. R_f = 0.46 (TLC, PE/EA, 5:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.42 (s, 6H), 1.65−1.75 (m, 2H), 1.77−1.87 (m, 2H), 2.31 (s, 3H), 2.82 (s, 2H), 7.07−7.10 (m, 4H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 16.6, 18.9, 21.0, 24.7, 30.9, 36.3, 51.7, 93.7, 107.5, 128.8, 131.1, 133.2, 136.4. Anal. Calcd $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.14; H, 7.71. HRMS (ESI): *m*/*z* $[M + NH_4]^+$ calcd for $[C_{17}H_{26}NO_4]^+$ 308.1856; found 308.1856.

3,6,7a-Trimethyl-3a-(4-nitrobenzyl)tetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran, 2h. White crystals. Mp = 149−150 °C. R_f = 0.20 (TLC, PE/EA, 5:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.41 (s, 6H), 1.69−1.77 (m, 2H), 1.80−1.88 (m, 2H), 2.96 (c, 2H), 7.42 (d, 2H, *J* = 8.8 Hz), 8.15 (d, 2H, *J* = 8.8 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 16.7, 19.0, 24.5, 30.7, 36.7, 51.8, 93.8,

dx.doi.org/10.1021/jo202437r | J. Org. Chem. 2012, 77, 1833−1842

107.2, 123.3, 131.9, 144.4, 146.9. Anal. Calcd $C_{16}H_{19}NO_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 59.74; H, 6.07; N, 4.33. HRMS (ESI): m/z $[M + H]^+$ calcd for $[C_{16}H_{20}NO_6]^+$ 322.1285; found 322.1284.

3-(3,6,7a-Trimethylhexahydro-3,6-epoxy[1,2]dioxolo[3,4-*b*]-pyran-3a-yl)propanenitrile, 2i. White crystals. Mp = 114−115 °C. R_f = 0.13 (TLC, PE/EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.47 (s, 6H), 1.67−1.73 (m, 4H), 1.80−1.88 (m, 2H), 2.56−2.64 (m, 2H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 12.9, 15.6, 20.5, 24.5, 28.1, 30.5, 50.2, 94.3, 106.2, 119.5. Anal. Calcd $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.36; H, 7.22; N, 5.87. HRMS (ESI): m/z $[M + H]^+$ calcd for $[C_{12}H_{18}NO_4]^+$ 240.1230; found 240.1231.

3,6,7a-Trimethyl-3a-(prop-2-yn-1-yl)hexahydro-3,6-epoxy-[1,2]dioxolo[3,4-*b*]pyran, 2j. White crystals. Mp = 135−136 °C. R_f = 0.50 (TLC, PE/EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.50 (s, 6H), 1.71−1.79 (m, 2H), 1.92−2.00 (m, 2H) 2.04−2.09 (m, H), 2.36−2.42 (m, 2H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 16.0, 17.8, 20.7, 24.6, 30.7, 49.8, 72.2, 79.3, 94.5, 106.9. Anal. Calcd $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.29; H, 6.83. HRMS (ESI): m/z $[M + Na]^+$ calcd for $[C_{12}H_{16}NaO_4]^+$ 247.0941; found 247.0940.

3,6-Dimethyl-7a-phenyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran, 2k. White crystals. Mp = 75−76 °C. R_f = 0.5 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.47−1.86 (m, 10H), 2.65−2.69 (m, H), 7.32−7.45 (m, 3H), 7.52−7.62 (m, 2H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 12.5, 17.8, 24.8, 29.3, 50.8, 95.8, 105.5, 106.4, 126.7, 128.5, 129.4, 133.0. Anal. Calcd $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.70; H, 6.60. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{14}H_{17}O_4]^+$ 249.1119; found 249.1121.

3-(4-Bromophenyl)-6,7a-dimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran, 2l. White crystals. Mp = 122−123 °C. R_f = 0.34 (TLC, PE/EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.55 (s, 3H), 1.61 (s, 3H), 1.71−1.80 (m, 4H), 2.61−2.65 (m, H), 7.45 (d, 2H, J = 8.8 Hz), 7.53 (d, 2H, J = 8.8 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 12.4, 17.7, 24.8, 29.3, 50.7, 95.9, 105.5, 106.1, 123.9, 128.6, 131.7, 132.3. Anal. Calcd $C_{14}H_{15}BrO_4$: C, 51.40; H, 4.62; Br, 24.42. Found: C, 51.39; H, 4.63; Br, 24.29. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{14}H_{16}BrO_4]^+$ 327.0219; found 327.0226.

3-(4-Methoxyphenyl)-6,7a-dimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran, 2m. White crystals. Mp = 89−90 °C. R_f =0.52 (TLC, PE/EA, 2:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.55 (s, 3H), 1.61 (s, 3H), 1.68−1.80 (m, 4H), 2.62−2.66 (m, H), 3.80 (s, 3H), 6.90 (d, 2H, J = 8.8 Hz), 7.49 (d, 2H, J = 8.8 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 12.5, 17.9, 24.8, 29.3, 50.5, 55.3, 95.8, 105.6, 106.5, 113.9, 124.7, 128.1, 160.5. Anal. Calcd $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.73; H, 6.75. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{15}H_{19}O_5]^+$ 279.1227; found 279.1227.

3,6-Dimethyl-7a-(*p*-tolyl)hexahydro-3,6-epoxy[1,2]dioxolo-[3,4-*b*]pyran, 2n. White crystals. Mp = 105−106 °C. R_f = 0.38 (TLC, PE/EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.47−1.87 (m, 10H), 2.35 (s, 3H), 2.64−2.67 (m, H), 7.20 (d, 2H, J = 8.1 Hz), 7.46 (d, 2H, J = 8.1 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 12.5, 17.8, 21.2, 24.8, 29.3, 50.6, 95.8, 105.5, 106.5, 126.7, 129.2, 130.0, 139.8. Anal. Calcd $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.55; H, 6.81. HRMS (ESI): m/z $[M + Na]^+$ calcd for $[C_{15}H_{18}NaO_4]^+$ 285.1097; found 285.1096.

3-(4-Chlorophenyl)-6,7a-dimethylhexahydro-3,6-epoxy-[1,2]dioxolo[3,4-*b*]pyran, 2o. White crystals. Mp = 104−105 °C. R_f = 0.29 (TLC, PE/EA, 5:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.55 (s, 3H), 1.61 (s, 3H), 1.70−1.84 (m, 4H), 2.61−2.65 (m, H), 7.36 (d, 2H, J = 8.8 Hz), 7.52 (d, 2H, J = 8.8 Hz). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 12.4, 17.7, 24.8, 29.3, 50.7, 95.9, 105.5, 106.1, 128.3, 128.8, 131.7, 135.6. Anal. Calcd $C_{14}H_{15}ClO_4$: C, 59.48; H, 5.35; Cl, 12.54. Found: C, 59.47; H, 5.24; Cl, 12.55. HRMS (ESI): m/z $[M + K]^+$ calcd for $[C_{14}H_{15}ClKO_4]^+$ 321.0290; found 321.0290.

H_2SO_4-Catalyzed Reaction of Acetophenone 3 with Hydrogen Peroxide (Scheme 2). A 37% aqueous H_2O_2 solution (0.345 g, 3.75 mmol H_2O_2) and a solution of H_2SO_4 (1.0 g, 10 mmol) in EtOH (1 mL) were added with stirring to a solution of acetophenone **3** (0.30 g, 2.5 mmol) in EtOH (4 mL) at 10−15 °C. The reaction mixture was stirred at 20−25 °C for 1 h, and a mixture of CH_2Cl_2/PE = 2:1 (20 mL) was added. Then $NaHCO_3$ was added to the reaction mixture with stirring until the pH reached 7.0. The precipitate was filtered off. The filtrate was dried over Na_2SO_4, the precipitate was filtered off, and the solvent was removed in a water jet vacuum. After the isolation with the use of SiO_2, peroxide **4** was obtained in 27% yield (0.115 g, 0.68 mmol).

(1,1-Dihydroperoxyethyl)benzene, 4.[27] White crystals. Mp = 76−77 °C (Mp = 77−78 °C).[27] ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.69 (s, 3H), 7.30−7.43 (m, 3H), 7.49 (d, 2H, J = 7.3 Hz), 8.85 (br.s, 2H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 23.0, 111.3, 125.7, 128.5, 128.7, 138.1.

H_2SO_4-Catalyzed Reaction of 1-Phenylbutane-1,3-dione 5 with Hydrogen Peroxide (Scheme 2). A 37% aqueous H_2O_2 solution (0.256 g, 2.78 mmol H_2O_2) and a solution of H_2SO_4 (1.0 g, 10 mmol) in EtOH (1 mL) were added with stirring to a solution of diketone **5** (0.30 g, 1.85 mmol) in EtOH (4 mL) at 10−15 °C. The reaction mixture was stirred at 20−25 °C for 1 h, and a mixture of CH_2Cl_2/PE = 2:1 (20 mL) was added. Then $NaHCO_3$ was added to the reaction mixture with stirring until the pH reached 7.0. The precipitate was filtered off. The filtrate was dried over Na_2SO_4, the precipitate was filtered off, and the solvent was removed in a water jet vacuum. After the isolation with the use of SiO_2, a complex mixture of reaction products was obtained.

Synthesis of 3,6,7a-Trimethyl-3a-(oxiran-2-ylmethyl)-tetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran (6) from 3a-Allyl-3,6,7a-trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran (2e). MCPBA (0.656 g, 2.66 mmol) was added with stirring to a solution of **2e** (0.30 g, 1.33 mmol) in anhydrous CH_2Cl_2 (5 mL). The reaction mixture was kept at 20−25 °C for 24 h. Then CH_2Cl_2 (20 mL) was added, the organic layer was washed with water (2 × 10 mL), a 5% aqueous KOH solution (2 × 5 mL), and again with water (2 × 10 mL), dried over Na_2SO_4, and filtered. Then CH_2Cl_2 was removed in a water jet vacuum. The product was isolated by chromatography on SiO_2 using a PE/EA mixture as the eluent with a gradient of ethyl acetate from 20 to 50 vol %. Product **6** (0.30 g, 1.24 mmol), yield 93%.

3,6,7a-Trimethyl-3a-(oxiran-2-ylmethyl)tetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran, 6. White crystals. Mp = 61−62 °C. R_f = 0.46 (TLC, PE/EA, 1:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.40 (s, 3H), 1.48 (s, 3H), 1.54 (s, 3H), 1.65−1.95 (m, 6H), 2.43 (m, 1H), 2.78 (t, 1H, J = 4.4 Hz), 3.04−3.15 (m, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 16.0, 16.2, 19.2, 24.6, 30.7, 34.9, 47.2, 48.2, 50.7, 94.2, 106.9. Anal. Calcd $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.71; H, 7.28. HRMS (ESI): m/z $[M + K]^+$ calcd for $[C_{12}H_{18}KO_5]^+$ 281.0786; found 281.0783.

Synthesis of 3-(3,6,7a-Trimethyldihydro-3*H*,4*H*-3,6-epoxy-[1,2]dioxolo[3,4-*b*]pyran-3a-yl)propanoic Acid (7) from Ethyl 3-(3,6,7a-Trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran-3a-yl)propanoate (2f). A solution of KOH (0.196 g, 3.50 mmol) in water (2 mL) was added with stirring to a solution of ester **2f** (0.50 g, 1.75 mmol) in EtOH (5 mL) at 20−25 °C. The reaction mixture was stirred at 20−25 °C for 1 h. Water (15 mL) was added to the reaction mixture, the mixture was washed with CH_2Cl_2 (30 mL), the aqueous layer was acidified with H_2SO_4 (0.35 g, 3.50 mmol), and acid **7** was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with water (5 mL), dried over Na_2SO_4, and filtered. The solvent was removed in a water jet vacuum. Product **7** was isolated by chromatography on SiO_2 using a PE /EA mixture as the eluent with a gradient of ethyl acetate from 40 to 70 vol %. Product **7** (0.429 g, 1.66 mmol), yield 95%.

3-(3,6,7a-Trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo-[3,4-*b*]pyran-3a-yl)propanoic Acid, 7. White crystals. Mp = 146−147 °C. R_f = 0.70 (TLC, methanol). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.47 (s, 6H), 1.67−1.72 (m, 4H), 1.76−1.86 (m, 2H), 2.53−2.64 (M, 2H), 9.16 (br. s, H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 15.7, 20.1, 24.6, 26.3, 29.2, 30.7, 50.2, 94.2, 106.8, 179.1. Anal. Calcd $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.77; H, 6.90. HRMS (ESI): m/z $[M + K]^+$ calcd for $[C_{12}H_{18}KO_6]^+$ 297.0735; found 297.0734.

Synthesis of 4-[3-(3,6,7a-Trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran-3a-yl)propanoyl]morpholine (8) from 3-(3,6,7a-Trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran-3a-yl)propanoic Acid (7). Triethylamine (0.157 g, 1.55 mmol) and ethyl chloroformate (0.168 g, 1.55 mmol) were added with stirring to a solution of **7** (0.20 g, 0.78 mmol) in dry

dx.doi.org/10.1021/jo202437r | J. Org. Chem. 2012, 77, 1833−1842

CH_2Cl_2 (20 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h. Then morpholine (0.203 g, 2.33 mmol) was added. The reaction mixture was stirred at 0 °C for 1 h, CH_2Cl_2 (20 mL) was added, and the mixture was washed with water (10 mL), a 5% aqueous H_2SO_4 solution (2 × 10 mL), a 5% aqueous $NaHCO_3$ solution (2 × 10 mL), and water (1 × 10 mL). The organic layer was dried over Na_2SO_4 and filtered. The solvent was removed in a water jet vacuum. Product **8** was isolated by chromatography on SiO_2 using a PE/EA mixture as the eluent with a gradient of ethyl acetate from 40 to 80 vol %. Product **8** (0.193 g, 0.59 mmol), yield 76%.

4-[3-(3,6,7a-Trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo-[3,4-*b*]pyran-3a-yl)propanoyl]morpholine, 8. White crystals. Mp = 117−118 °C. R_f = 0.37 (TLC, EA). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.44 (s, 6H), 1.67−1.71 (m, 4H), 1.79−1.87 (m, 2H), 2.47−2.55 (m, 2H), 3.38−3.72 (m, 8H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 15.6, 21.3, 24.6, 27.1, 27.4, 30.8, 42.0, 45.6, 50.4, 66.6, 66.8, 94.2, 106.7, 177.2. Anal. Calcd $C_{16}H_{25}NO_6$: C, 58.70; H, 7.70; N, 4.28. Found: C, 58.71; H, 7.85; N, 4.29. HRMS (ESI): *m*/*z* $[M + K]^+$ calcd for $[C_{16}H_{25}KNO_6]^+$ 366.1313; found 366.1314.

Synthesis of *N*-(1-Adamantyl)-3-(3,6,7a-trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran-3a-yl)propanamide (9) from 3-(3,6,7a-Trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]-dioxolo[3,4-*b*]pyran-3a-yl)propanoic Acid (7). Triethylamine (0.390 g, 3.85 mmol) and ethyl chloroformate (0.168 g, 1.55 mmol) were added with stirring to a solution of **7** (0.20 g, 0.78 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, and then 1-adamantanamine hydrochloride (0.434 g, 2.31 mmol) was added. The mixture was stirred at 0 °C for 1 h. The isolation was performed as described in the synthesis of **8**. Product **9** (0.27 g, 0.69 mmol), yield 89%.

***N*-(1-Adamantyl)-3-(3,6,7a-trimethyldihydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran-3a-yl)propanamide, 9.** White crystals. Mp = 159−160 °C. R_f = 0.69 (TLC, PE/EA, 1:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.37 (s, 3H), 1.45 (s, 6H), 1.57−1.71 (m, 10H), 1.72−1.83 (m, 2H), 1.91−1.98 (m, 6H), 1.99−2.07 (m, 3H), 2.25−2.34 (M, 2H), 5.13 (br.s, 1H). ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 15.7, 20.7, 24.7, 27.0, 29.4, 30.8, 31.9, 36.3, 41.7, 50.5, 51.9, 94.1, 106.9, 171.4. Anal. Calcd $C_{22}H_{33}NO_5$: C, 67.49; H, 8.50; N, 3.58. Found: C, 67.68; H, 8.41; N, 3.47. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $[C_{22}H_{34}NO_5]^+$: 392.2431; found 392.2427.

Bromination of 3a-Allyl-3,6,7a-trimethyltetrahydro-3*H*,4*H*-3,6-epoxy[1,2]dioxolo[3,4-*b*]pyran (2e). A solution of Br_2 (0.20 g, 1.27 mmol) in CH_2Cl_2 (5 mL) was added dropwise with stirring to a solution of tricyclic peroxide **2e** (0.30 g, 1.15 mmol) in CH_2Cl_2 (10 mL) at 70 °C. The reaction mixture was stirred at 0 °C for 30 min. Then CH_2Cl_2 was removed in a water jet vacuum. After the isolation with the use of SiO_2, the target dibrominated peroxide was not obtained; instead, a complex mixture of reaction products formed.

Reduction of 9-Benzyl-1,4,6-trimethyl-2,3,5,10-tetraoxatricyclo[4.3.1.0^{4,9}]decane 2c with Triphenylphosphine. Triphenylphosphine (181 mg, 0.69 mmol) was added to a solution of tricyclic peroxide **2c** (60 mg, 0.23 mmol) in $CDCl_3$ (0.8 mL). The course of the reaction was monitored in an NMR tube. Only signals of triketone **1c** were observed 24 h after the mixing of the reagents. Triketone **1c** was isolated in 92% yield (58 mg, 0.21 mmol).

General Procedures for the Determination of Stability Tricyclic Peroxides. Tricyclic peroxide **2c** (0.30 g, 1.09 mmol) was dissolved in EtOH (4 mL), refluxed for 1 h, and cooled. Then EtOH was removed in a water jet vacuum. Tricyclic peroxide **2c** was isolated (0.293 g, 1.06 mmol); the yield was 97% based on the staring reagent.

Sulfuric acid (80 mg, 0.8 mmol) was added with stirring to a solution of tricyclic peroxide **2c** (0.30 g, 1.09 mmol) in EtOH (4 mL) at 10−15 °C. The mixture was refluxed for 1 h and then cooled. A mixture of CH_2Cl_2/PE = 1:1 (10 mL) was added to the reaction mixture, and then $NaHCO_3$ was added until the pH reached 7.0. The precipitate was filtered off. The filtrate was dried over Na_2SO_4 and filtered. The solvent was removed in a water jet vacuum. According to the NMR spectroscopic data, the reaction mixture did not contain tricyclic peroxide **2c**.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of β,δ-triketones **1**; ^{1}H and ^{13}C NMR spectra and mass spectra of tricycles **2**, **7**−**9**; and details of X-ray data for **2b** and **2l**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel: +7 (499) 1356428. Fax: +7 (499) 1355328. E-mail: terentev@ioc.ac.ru.

■ ACKNOWLEDGMENTS

This work is supported by the Program for Support of Leading Scientific Schools of the Russian Federation (Grant NSh 4659.2012.3), the Grant of the Russian Foundation for Basic Research (Grant 11-03-00857-a), and the Ministry of education and science of the Russian Federation (Grant 16.513.11.3108).

■ REFERENCES

(1) Denisov, E. T.; Denisova, T. G.; Pokidova, T. S. *Handbook of Free Radical Initiators*; John Wiley and Sons: New York, 2003.

(2) (a) Jefford, C. W. *Drug Discovery Today* **2007**, *12*, 487−495. (b) Opsenica, D. M.; Šolaja, B. A. *J. Serb. Chem. Soc.* **2009**, *74*, 1155−1193. (c) Muregi, F. W.; Ishih, A. *Drug Dev. Res.* **2010**, *71*, 20−32. (d) Muraleedharan, K. M.; Avery, M. A. *Drug Discovery Today* **2009**, *14*, 793−803. (e) O'Neill, P. M.; Posner, G. H. *J. Med. Chem.* **2004**, *47*, 2945−2964. (f) Dong, Y. *Mini-Rev. Med. Chem.* **2002**, *2*, 113−123. (g) Vennerstrom, J. L.; Fu, H.-N.; Ellis, W. Y.; Ager, A. L.; Wood, J. K.; Andersen, S. L.; Gerena, L.; Milhous, W. K. *J. Med. Chem.* **1992**, *35*, 3023−3027. (h) Barton, V.; Ward, S. A.; Chadwick, J.; Hill, A.; O'Neill, P. M. *J. Med. Chem.* **2010**, *53*, 4555−4559. (I) Ghorai, P.; Dussault, P. H.; Hu, C. *Org. Lett.* **2008**, *10*, 2401−2404. (j) Tolstikov, G. A.; Tolstikov, A. G.; Tolstikova, O. V. *Russ. Chem. Rev.* **1996**, *65*, 769−783.

(3) (a) Keiser, J.; Veneziano, V.; Rinaldi, L.; Mezzino, L.; Duthaler, U.; Cringoli, Gi. *Res. Vet. Sci.* **2010**, *88*, 107−110. (b) Shuhua, X.; Tanner, M.; N'Goran, E. K.; Utzinger, J.; Chollet, J.; Bergquist, R.; Chen, M.; Zheng, J. *Acta Trop.* **2002**, *82*, 175−181. (c) Keiser, J.; Brun, R.; Fried, B.; Utzinger, J. *Antimicrob. Agents Chemother.* **2006**, *50*, 803−805. (d) Keiser, J.; Xiao, S. H.; Tanner, M.; Utzinger, J. *J. Antimicrob. Chemother.* **2006**, *57*, 1139−1145.

(4) (a) Dembitsky, V. M.; Gloriozova, T. A.; Poroikov, V. V. *Mini-Rev. Med. Chem.* **2007**, *7*, 571−589. (b) Jung, M.; Kim, H.; Lee, K.; Park, M. *Mini-Rev. Med. Chem.* **2003**, *3*, 159−165. (c) Kim, J.; Park, E. J. *Curr. Med. Chem. Anticancer Agents* **2002**, *2*, 485−537. (d) Dembitsky, V. M. *Eur. J. Med. Chem.* **2008**, *43*, 223−251. (e) Terzić, N.; Opsenica, D.; Milić, D.; Tinant, B.; Smith, K. S.; Milhous, W. K.; Šolaja, B. A. *J. Med. Chem.* **2007**, *50*, 5118−5127. (f) Žižak, Ž.; Juranić, Z.; Opsenica, D.; Šolaja, B. A. *Invest. New Drugs* **2009**, *27*, 432−439.

(5) *Organic Peroxides*; Swern, D., Ed.; Wiley-Interscience: New York, 1971; Vol. 2.

(6) (a) Milas, N. A.; Mageli, O. L.; Golubović, A.; Arndt, R. W.; Ho, J. C. J. *J. Am. Chem. Soc.* **1963**, *85*, 222−226. (b) Rieche, A.; Bischoff, C. *Chem. Ber.* **1962**, *95*, 77−82. (c) Cocker, W.; Grayson, D. H. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1347−1352. (d) Vinogradova, L. P.; Zav'yalov, S. I. *Izvest. Akad. Nauk. S.S.S.R., Ser. Khim.* **1961**, 1482−1486 ; *Chem. Abstr.* **1962**, *56*, 338b. (e) Vinogradova, L. P.; Zav'yalov, S. I. *Izvest. Akad. Nauk. S.S.S.R., Ser. Khim.* **1961**, 2050−2054 ; *Chem. Abstr.* **1962**, *57*, 12344c. (f) Vinogradova, L. P.; Rudenko, B. A.; Zav'yalov, S. I. *Izvest. Akad. Nauk. S.S.S.R., Ser. Khim.* **1962**, 1436−1441 ; *Chem. Abstr.* **1963**, *58*, 2378g. (g) Rieche, A.; Eberhard, S.; Brand, F. *Liebigs. Ann. Chem.* **1969**, *725*, 93−98. (h) Opsenica, D.; Pocsfalvi, G.; Milhous, W. K.; Solaja, B. A. *J. Serb. Chem. Soc.* **2002**, *67*, 465−471.

(7) Rieche, A.; Bischoff, C.; Prescher, D. *Chem. Ber.* **1964**, *97*, 3071−3075.
(8) (a) Zmitek, K.; Zupan, M.; Stavber, S.; Iskra, J. *J. Org. Chem.* **2007**, *72*, 6534−6540. (b) Terent'ev, A. O.; Kutkin, A. V.; Platonov, M. M.; Ogibin, Yu. N.; Nikishin, G. I. *Tetrahedron Lett.* **2003**, *44*, 7359−7364. (c) Jefford, C. W.; Li, Y.; Jaber, A.; Boukouvalas, J. *Synth. Commun.* **1990**, *20*, 2589−2596.
(9) Kocienski, P. J. *Protecting Groups*; Thieme: New York, 2003.
(10) (a) McCullough, K. J.; Ushigoe, Y.; Tanaka, S.; Kawamura, S.; Masuyama, A.; Nojima, M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3059−3064. (b) Sugimoto, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1990**, *112*, 3690−3692.
(11) (a) Zmitek, K.; Zupan, M.; Stavber, S.; Iskra, J. *Org. Lett.* **2006**, *8*, 2491−2494. (b) Azarifar, D.; Khosravi, K.; Soleimanei, F. *Synthesis* **2009**, 2553−2556.
(12) Li, Y.; Hao, H.-D.; Wu, Y. *Org. Lett.* **2009**, *11*, 2691−2694.
(13) Li, Y.; Hao, H.-D.; Zhang, Q.; Wu, Y. *Org. Lett.* **2009**, *11*, 1615−1618.
(14) Yan, X.; Chen, J.; Zhu, Y.-T.; Qiao, C. *Synlett* **2011**, 2827−2830.
(15) (a) Baeyer, A.; Villiger, V. *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 3625−3633. (b) Baeyer, A.; Villiger, V. *Ber. Dtsch. Chem.Ges.* **1900**, *33*, 858−864. (c) Krow, G. R. *Organic Reactions*; Paquette, L., Ed.; John Wiley and Sons: New York, 1993; Vol. *43*, pp 251−798. (d) Renz, M.; Meunier, B. *Eur. J. Org. Chem.* **1999**, 737−750. (e) Belov, V. N.; Heyfitz, L. A.; Virezub, S. I. Reaczii, I *Metodi issledovaniya organicheskich soedineniy*; Goshimizdat: Moscow, **1961**; Vol. *10*, pp 7−208.
(16) (a) Criegee, R. *Ber. Dtsch. Chem. Ges.* **1931**, *64*, 260. (b) Criegee, R. *Ber. Dtsch. Chem. Ges.* **1944**, *77*, 722. (c) Michailovici, M. L. *Synthesis* **1970**, 209. (d) Ogibin, Y. N.; Terent'ev, A. O.; Kutkin, A. V.; Nikishin, G. I. *Tetrahedron Lett.* **2002**, *43*, 1321−1324.
(17) (a) Hock, H.; Lang, S. *Ber. Dtsch. Chem. Ges* **1944**, *B77*, 257. (b) Jordan, W.; van Barneveld, H.; Gerlich, O.; Boymann, M. K.; Ullrich, J. In *Ullmanns Encyclopedia of Industrial Organic Chemicals*; Gerhartz, W., Ed.; Wiley-VCH: Weinheim, 1985; Vol. *A9*, pp 299−312. (c) Nakamura, R.; Obora, Y.; Ishii, Y. *Chem. Commun.* **2008**, 3417.
(18) Terent'ev, A. O.; Borisov, D. A.; Chernyshev, V. V.; Nikishin, G. I. *J. Org. Chem.* **2009**, *74*, 3335−3340.
(19) Terent'ev, A. O.; Krivykh, O. V.; Krylov, I. B.; Ogibin, Yu. N.; Nikishin, G. I. *Russ. J. Gen. Chem.* **2010**, *80*, 1667−1671.
(20) (a) Adam, W.; Blancafort, L. *J. Org. Chem.* **1997**, *62*, 1623−1629. (b) Clennan, E. L.; Heah, P. C. *J. Org. Chem.* **1982**, *47*, 3329−3331. (c) Clennan, E. L.; Heah, P. C. *J. Org. Chem.* **1981**, *46*, 4105−4107. (d) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1984**, *49*, 793−798.
(21) (a) Terent'ev, A. O.; Platonov, M. M.; Krylov, I. B.; Chernyshev, V. V.; Nikishin, G. I. *Org. Biomol. Chem.* **2008**, *6*, 4435−4441. (b) Ito, T.; Tokuyasu, T.; Masuyama, A.; Nojima, M.; McCullough, K. J. *Tetrahedron* **2003**, *59*, 525−536. (c) Dussault, P. H.; Lee, I. Q. *J. Am. Chem. Soc.* **1993**, *115*, 6458−6459. (d) Dussault, P. H.; Eary, C. T. *J. Am. Chem. Soc.* **1998**, *120*, 7133−7134. (e) Dussault, P. H.; Lee, H. J.; Niu, Q. J. *J. Org. Chem.* **1995**, *60*, 784−785. (f) Dussault, P. H.; Zope, U. R. *J. Org. Chem.* **1995**, *60*, 8218−8222. (f) Terent'ev, A. O.; Borisov, A. M.; Platonov, M. M.; Starikova, Z. A.; Chernyshev, V. V.; Nikishin, G. I. *Synthesis* **2009**, 4159−4166.
(22) (a) Wuts, P. G. M.; Greene, T. W. *Greene's Protective Groups in Organic Synthesis*, 4th ed.; Wiley-Interscience: New York, 2006. (b) Torok, D. S.; Figueroa, J. J.; Scott, W. J. *J. Org. Chem.* **1993**, *58*, 7274−7276. (c) Vyvyan, J. R.; Meyer, J. A.; Meyer, K. D. *J. Org. Chem.* **2003**, *68*, 9144−9147.
(23) Belyakov, P. A.; Kadentsev, V. I.; Chizhov, A. O.; Kolotyrkina, N. G.; Shashkov, A. S.; Ananikov, V. P. *Mendeleev Commun.* **2010**, *20*, 125−131.
(24) Christoffers, J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3141−3149.
(25) Bartoli, G.; Bosco, M.; Bellucci, M. C.; Marcantoni, E.; Sambri, L.; Torregiani, E. *Eur. J. Org. Chem.* **1999**, *3*, 617−620.
(26) Shirakawa, S.; Shimizu, S. *Synlett* **2007**, *20*, 3160−3164.
(27) (a) Das, B.; Krishnaiah, M.; Veeranjaneyulu, B.; Ravikanth, B. *Tetrahedron Lett.* **2007**, *48*, 6286−6289. (b) Tada, N.; Cui, L.; Okubo, H.; Miura, T.; Itoh, A. *Adv. Synth. Catal.* **2010**, *352*, 2383−2386.