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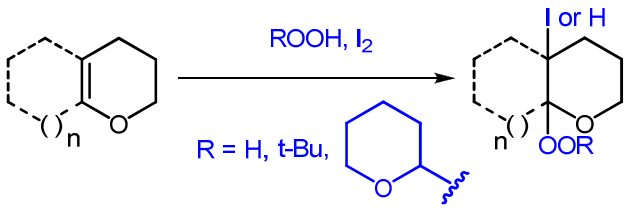

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PAPER

Reactions of Mono- and Bicyclic Enol Ethers with the I_2 – Hydroperoxide System

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Reactions of mono- and bicyclic enol ethers with I_2–H_2O_2, I_2–Bu^{t}OOH, and I_2–tetrahydropyranyl hydroperoxide systems have been studied. It was shown that the reaction pathway depends on the nature of peroxide and the ring size. The reaction of 2,3-dihydrofuran and 3,4-dihydro-2*H*-pyran with the I_2 - hydroperoxide system affords iodoperoxides, α-iodolactones, and α-iodohemiacetals. Bicyclic enol ethers are transformed into vicinal iodoperoxides only in the reaction with the I_2–H_2O_2 system, whereas the reaction with I_2–Bu^{t}OOH gives the hydroperoxidation product.

Introduction

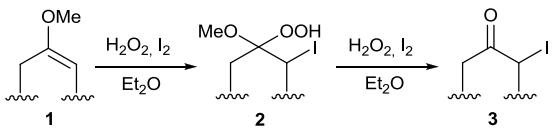
In the last decades an extensive development of methods for the synthesis of organic peroxides is observed, for example, such catalysts in combination with hydroperoxides are used as H_2WO_4,[1] phosphomolybdic and phosphotungstic acids,[2] methyltrioxorhenium ($MeReO_3$) in trifluoroethanol,[3] trifluroacetic acid with cinchona alkaloids,[4] Re_2O_7,[5] BF_3•Et_2O,[6] CAN,[7] silicon-supported sodium hydrogen sulfate,[8] camphorsulfonic acid,[9] $SrCl_2 \cdot 6H_2O$,[10] and also salts of ruthenium,[11] copper,[12] cobalt,[13] and iron,[14] including Gif [15] and metalloporphyrin [16] systems. This development is associated with the fact that many compounds of this class exhibit pronounced antimalarial and anthelmintic activities.[17] Some synthesized compounds show antiparasitic activity comparable to or higher than that of the natural peroxide artemisinin commonly used in medical practice.[18] The search for natural substances and the synthesis of new compounds with antitumor activity is a relatively new and fast-developing field of application of this class of compounds.[19] Peroxides are widely used in the polymer chemistry as radical polymerization initiators and cross-linking reagents.[20] These aspects of the application of compounds containing the -O-O- moiety stimulated the development of new approaches to their synthesis.

However, despite the more than a hundred year history of the development of this field of chemistry, the selective synthesis and the controlled transformation of peroxides, as well as their analysis, still present difficulties due to low stability of these compounds (compared to other classes) and the fact that they easily undergo decomposition by a homolytic or heterolytic mechanism.

The present study is in the line with the current trends of using the I_2-H_2O_2 system for the peroxidation and halogenation of organic compounds. This system shows unique and unpredictable reactivity, which is manifested in the fact that the reactions with this system afford a great variety of products. An idea of the combination of iodine or its compounds with peroxides was successfully implemented for the introduction of the peroxide moiety into carbonyl compounds[21] and alkenes,[22] in the synthesis of monoperoxyacetal-containing compounds[23] and cyclic triperoxides,[24] for the activation and introduction of iodine in the iodoalkoxylation of alkenes,[25] the iodination of arenes,[26] ketones,[27] and alkynes.[28] Besides, this system was used for the Baeyer–Villiger oxidation of ketones to lactones,[29] the ring contraction of 1,2-quinones to form cyclopentenones,[30] the oxidative C-N[31] and C-O[32] coupling, and the oxidative cyclization to form heterocyclic compounds.[33]

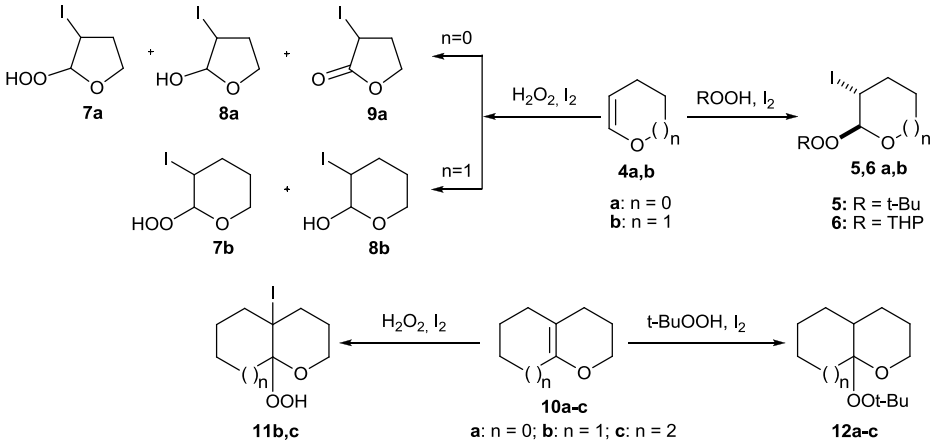
The results of investigations covering the iodination of organic compounds or iodine-catalyzed transformations, including peroxides, are summarized in reviews.[34, 35, 36]

In our previous study we showed that the reaction of enol ethers **1** (containing an exocyclic oxygen atom) with the I_2-H_2O_2 system in Et_2O produces 2-iodo-1-methoxyhydroperoxides **2** and 2-iodoketones **3**. Depending on the reaction conditions, either compounds **2** or **3** can be synthesized in preparative yield (Scheme 1).[37]



Scheme 1. Synthesis of 2-iodo-1-methoxyhydroperoxides **2** and 2-iodo ketones **3**.

In the present study, we focused our attention on another type of enol ethers, featuring an endocyclic oxygen atom (**4a,b** and **10a-c**). Contrary to expectations, cyclic enol ethers **4a,b** and **10a-c** show substantially different behaviour in the reaction with the iodine-hydroperoxide system compared to their acyclic analogues **1** (Scheme 2).



Scheme 2. Reactions of cyclic enol ethers **4a, b**, and **10a-c** with the iodine-hydroperoxide system.

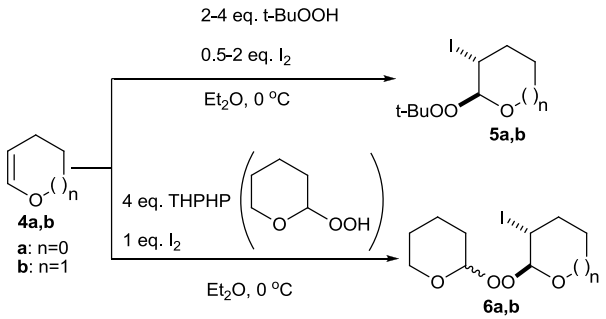
We studied two groups of enol ethers – monocyclic enol ethers, such as 2,3-dihydrofuran **4a** and 3,4-dihydro-2*H*-pyran **4b**, and more complex compounds, such as bicyclic enol ethers, in which a five-membered **10a**, six-membered **10b**, or seven-membered **10c** carbocycle is fused with the dihydropyran ring.

Reactions of 2,3-dihydrofuran 4a and 3,4-dihydro-2*H*-pyran 4b with the iodine - H_2O_2 system

The reaction of dihydrofuran **4a** with the iodine - H_2O_2 system at 0 °C affords a complex mixture of products consisting of iodohydroperoxide **7a** (yield 65%), α-iodolactone **9a** (yield 15%), and hemiacetal **8a** (yield 15%). The reaction of dihydropyran **4b** with the iodine - H_2O_2 system produced a mixture of iodohydroperoxide **7b** (yield 74%) and hemiacetal **8b** (yield 12%), the expected iodovalerolactone was not detected. Apparently, this is associated with the fact that δ-valerolactone, unlike γ-butyrolactone, easily polymerizes.[38]

Reactions of 2,3-dihydrofuran 4a and 3,4-dihydro-2*H*-pyran 4b with the iodine – *tert*-butyl (TBHP) and iodine – tetrahydropyranyl hydroperoxide (THPHP) systems.

The iodoperoxidation of 2,3-dihydrofuran (Table 1, entries 1-7) **4a** and 3,4-dihydropyran **4b** (Table 1, entries 8-14) was performed in Et_2O, CH_3CN, or CH_3CN - Et_2O using a two- or fourfold molar excess of TBHP (Table 1, entries 1-5 and 8-11) or a fourfold molar excess of THPHP (Table 1, entries 6-7 and 12-14) and iodine (0.5-2 mole per mole of **4**). To suppress the oxidative side reactions, the synthesis was performed at 0 °C (Scheme 3, Table 1).



Scheme 3. Reactions of 2,3-dihydrofuran **4a** and 3,4-dihydro-2*H*-pyran **4b** with the I_2 – TBHP and I_2 – THPHP systems.

Table 1. Reactions of 2,3-dihydrofuran **4a** and 3,4-dihydro-2*H*-pyran **4b** with the I_2 – TBHP and I_2 – THPHP systems; synthesis of peroxides **5a,b** and **6a,b**.

Entry [a]	Solvent	ROOH	Molar ratio: I_2 / **4a,b**	Reaction time, min	Yield of **5a,b** and **6a,b**, %
1	Et_2O	TBHP	0.5 (**4a**)	30	28 (**5a**)
2	Et_2O	TBHP	1 (**4a**)	30	76 (**5a**)
3	Et_2O	TBHP	2 (**4a**)	30	56 (**5a**)
4	Et_2O	TBHP	2 (**4a**)	30	77 (**5a**)
5	CH_3CN - Et_2O	TBHP	2 (**4a**)	30	52 (**5a**)
6	Et_2O	THPHP	1 (**4a**)	120	78 (**6a**)
7	CH_3CN	THPHP	1 (**4a**)	120	35 (**6a**)
8	Et_2O	TBHP	1 (**4b**)	30	91 (**5b**)
9	Et_2O	TBHP	1 (**4b**)	120	88 (**5b**)
10	CH_3CN - Et_2O	TBHP	1 (**4b**)	30	56 (**5b**)
11 [b]	Et_2O	TBHP	1 (**4b**)	30	17 (**5b**)
12	Et_2O	THPHP	1 (**4b**)	120	86 (**6b**)
13	Et_2O	THPHP	1 (**4b**)	30	42 (**6b**)
14	CH_3CN	THPHP	1 (**4b**)	120	46 (**6b**)

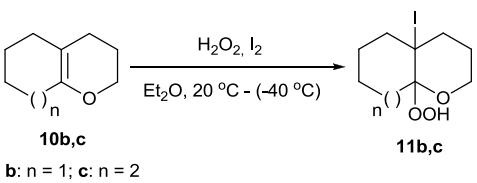
[a] Molar ratio: ROOH / **4a,b** = 4 (entries 1-3, 5-14) and 2 (entry 4); [b] At 20-25°C.

The highest yield of products **5a** (76%) and **5b** (91%) was achieved

when the reaction was performed for 30 min (Table 1, entries 2 and 8) in the presence of an equivalent amount of iodine. An increase in the reaction time to 2 h had no substantial effect of the yield of **5b** (Table 1, entry 9). The use of a twofold excess of iodine led to a decrease in the yield of **5a** to 56% (Table 1, entry 3). A decrease in the amount of TBHP (Table 1, entry 4) compared to entry 2 had no effect on the yield of the product. The replacement of Et_2O (the reaction medium) by more polar solvent CH_3CN or a CH_3CN - Et_2O mixture led to a sharp decrease in the yield of **5a,b** and **6a,b** (entries 5, 7, 10, and 14). The reaction with the use of THPHP requires 2 h for the synthesis of **6a,b** to be efficient (Table 1, entries 6 and 12). On the whole, the yields of dihydrofuran derivatives **5a** and **6a** (Table 1, entries 1-7) are lower compared to their dihydropyran homologs **5b** and **6b** (Table 1, entries 8-14). At room temperature, dihydropyran polymerizes under the action of the reaction system used, which leads to a decrease in the yield of **5b** (Table 1, entry 11).

Reaction of bicyclic enol ethers 10b,c with the I_2-H_2O_2 system

One important feature to consider when comparing mono- and bicyclic enol ethers is the absence of hydrogen atoms near double bond in the later systems. Usually peroxides containing $R_2(R'O)COOH$ fragment are more stable than R_2HCOOH peroxides, since they have no easily oxidizable CH fragment. This difference in stability is observed in acid-catalyzed peroxidation of aldehydes and ketones or their acetals [6] with hydrogen peroxide. It is common knowledge that aldehydes can be easily oxidated by H_2O_2 in carboxylic acids, in contrast more rigid conditions are needed for oxidation of ketons by H_2O_2 with the same result.[39] In the case of base-catalyzed processes, R_2HCOOH peroxides can be rearranged in ketones by means of Kornblun-DeLaMare reaction.[40] Apparently, this is the reason why iodohydroperoxides of bicyclic enol ethers **10b,c** are formed more selectively than analogous peroxides of monocyclic enol ethers **4a,b**, which undergo further transformations (Scheme 4).



Scheme 4. Reaction of bicyclic enol ethers **10b,c** with the I_2-H_2O_2 system.

Table 2. Reaction of bicyclic enol ethers **10b,c** with the I_2-H_2O_2 system; synthesis of iodohydroperoxides **11b,c**.

Entry	Bicyclic enol ethers **10b,c**	Solvent	Onset temperature of the reaction, °C	Yield of **11b,c**, %
15	**10b**	Et_2O	20	**11b**, 10
16	**10b**	Et_2O	0	**11b**, 43
17	**10b**	Et_2O	-40	**11b**, 82
18	**10b**	CH_3CN	20	**11b**, traces
19	**10b**	CH_3CN	-40	**11b**, traces
20	**10c**	Et_2O	-40	**11c**, 40

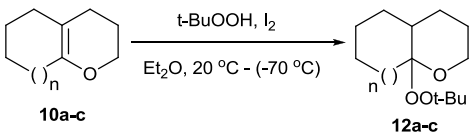
The conditions of the peroxidation of bicyclic ethers **10b,c** (Table 2, entries 15-20) were optimized taking into account the conditions of entry 2 (Table 1). The most significant parameters, *viz.*, the temperature and the reaction medium, were varied. As the temperature was lowered from room temperature to -40 °C, the yield of target product **11b** increased from trace amounts to 82% (Table 2, entries 15-17) due, apparently, to the reduction of the effect of polymerization with the participation of enol ether. The reaction in CH_3CN (Table 2, entries 18 and 19) produces virtually no iodohydroperoxide **11b**.

Iodohydroperoxides **11b,c** are unstable compounds and they decompose during isolation and storage.

Reaction of bicyclic enol ethers 10a-c with the I_2-Bu^{t}OOH system.

TBHP is much more bulky than hydrogen peroxide, which has a decisive effect on the structure of the reaction products. Thus, *tert*-butyl hydroperoxide adds at the double bond, whereas iodine is not involved in the final product.

The reactions of bicyclic ethers **10a-c** with the I_2-Bu^{t}OOH system were performed using a fourfold molar excess of TBHP and an equimolar amount of iodine, with the resulting formation of peroxidated oxabicycloalkanes **12a-c** (Scheme 5, Table 3).



Scheme 5. Reaction of bicyclic enol ethers **10a-c** with the I_2-Bu^{t}OOH system.

Table 3. Reaction of bicyclic ethers **10a-c** with the I_2-Bu^{t}OOH system; synthesis of peroxides **12a-c**.

Entry	Bicyclic enol ethers **10b,c**	Solvent	Onset temperature of the reaction, °C	Yield of **12 a-c**, %
21	**10a**	Et_2O	-70	**12a,** 89
22	**10b**	Et_2O	20	**12b,** 43
23	**10b**	Et_2O	0	**12b**, 51
24	**10b**	Et_2O	-40	**12b**, 70
25	**10b**	Et_2O	-70	**12b**, 75
26	**10b**	CH_3CN	-70	**12b**, traces
27	**10c**	Et_2O	-70	**12c**, 66

In the reaction with the I_2-Bu^{t}OOH system, like in the reaction with I_2-H_2O_2, the temperature and the nature of the solvent (Table 3, entries 21-27) play a key role in the synthesis of target peroxide **12**. In entries 22-25 (Table 3), the yield of the target peroxide increased from 43 to 75% as the reaction temperature was lowered from 20 to -70 °C. Acetonitrile (Table 3, entry 26) proved to be unsuitable as a solvent for the synthesis of **12b**. Products **12a-c** are more stable compared to **11a-c**; however, these compounds substantially decompose during storage even at 0 °C for one week.

Summary from the Tables 1-3 about influence of type of mono- and bicyclic enol ether, hydroperoxide, and solvent on the structure of the products

It is known that particles with positively charged iodine and protons are formed in the iodine - hydroperoxide system. [28a, 41] Both these positively charged particles, as well as iodine add at the double bond of enol ether thus initiating the peroxidation. The reactions

with dihydrofuran and dihydropyran are accompanied by the iodoperoxidation. In the case of bicylic compounds, the iodoperoxidation is observed only in the reactions with hydrogen peroxide. The reactions with more bulky TBHP involve the addition of only this compound, whereas iodine is not involved in the resulting peroxide. In the reactions with THPHP, no peroxidation of bicyclic compounds is observed.

In addition to the formation of iodohydroperoxide **7a**, the reaction of dihydrofuran with the I_2-H_2O_2 system involves the reduction of the hydroperoxide group with HI giving iodo alcohol **8a** [42] and the oxidation of **8a** with iodine or particles containing positively charged iodine producing iodolactone **9a**.[43]

Diethyl ether proved to be a much more efficient solvent compared to acetonitrile, because it is a good base, an acceptor of a proton or positively charged iodine, due to which the synthesis can be performed in a relatively milder acidic medium. The reaction in acetonitrile yields mainly resinification products due, apparently, to the acid-catalyzed polymerization characteristic of enol ethers.[44]

Establishment of the structures of the synthesized compounds

The structures of products **5, 6, 11**, and **12** were established by ^{1}H and ^{13}C NMR spectroscopy. The ^{1}H NMR spectra of products **5** and **6** show characteristic signals of the CHI group and the peroxyacetal moiety at δ 3.7-4.15 and 4.9-5.7, respectively. The signal of the CH_2O group is observed at δ 3.5-4.0. Signals of other CH_2 groups are present in the characteristic region at δ 1.2-2.5.

In the ^{13}C NMR spectra, the signal of the monoperoxyacetal moiety is observed at δ 103-113, which is consistent with the known data.[45] The spectra of peroxides **5** show the signal of the tertiary carbon atom of the *tert*-butylperoxide group at δ 79 - 81. The spectra of peroxides **6** display several signals of the peroxiacetal moiety due to the formation of different steteroisomers. The ^{13}C NMR spectra show signals of the CH_2O group at δ 60-67 ppm and signals of other CH_2 groups at δ 24-36. The chemical shifts of the CHI group in the ^{13}C NMR spectra substantially depend on the environment of the carbon atom. In the spectra of products **5** and **6**, the signals of this group are observed at δ 19-23, whereas the signals for products **11** containing the tertiary carbon atom are shifted downfield (to δ 65-76).

The structures of compounds **7a, 8a, 9a**, and **7b, 8b**, which were not isolated in the individual state, were unambiguously established by ^{1}H and ^{13}C NMR spectroscopy using 2D correlation spectroscopic techniques (COSY, NOESY, editing-HSQC, HSQC-TOCSY, and HMBC). The molecular skeleton was established based on heteronuclear correlations. The O–CH–OOH and O–CH–OH groups in cyclic compounds **7a, 8a**, and **7b, 8b** differ by the chemical shifts in the ^{13}C NMR spectra. It is known [46] that the replacement of one alkoxy group in acetal by the peroxide group leads to a shift of the signal of the carbon atom in the O-C-O group to lower field. The same dependence was observed in the present study. Based on the HSQC NMR data, the chemical shifts for hydroperoxides are 105 ppm (**7a**) and 98 ppm (**7b**), whereas the chemical shifts for hemiacetals are observed at lower field (98 ppm for **8a** and 93 ppm for **8b**). The similar dependence is observed in the ^{1}H NMR spectra; for hydroperoxides, the chemical shifts are 5.6 ppm (**7a**) and 4.9 ppm (**7b**); for hemiacetal, the corresponding values are lower (4.8 ppm for **8a** and 4.1 ppm for **8b**).

The IR spectra of peroxides **5**, **6**, and **11** show characteristic CH–I stretching bands in the region of 500–800 cm^{-1} and CH–O stretching bands of the peroxyketal moiety in the region of 1020–1300 cm^{-1}.

The compositions of the synthesized compounds were established also using HRMS data. The mass spectra of **5**, **6**, and **12** have peaks corresponding to the molecular ions. According to the mass-spectrometric data, the ES ionization of **11** leads to the elimination of the peroxide moiety **11b** or iodine atom and peroxide moiety **11c**.

Conclusions

The reactions of mono- and bicyclic enol ethers with the I_2–H_2O_2, I_2–Bu^{t}OOH, and I_2–tetrahydropyranyl hydroperoxide systems were studied. We succeeded in synthesizing and characterizing difficult-to-synthesize unstable oxacyclic peroxides and iodoperoxides. It was shown that the reaction pathway depends on the nature of peroxide and the ring size. The reaction of monocyclic enol ethers with the I_2 – H_2O_2 system produces iodoperoxides, α-iodohemiacetals, and α-iodolactones, whereas the reaction with I_2–Bu^{t}OOH gives only iodoperoxidation products. Bicylic enol ethers are transformed into vicinal iodoperoxides in 40 - 82% yields only in the reactions with the I_2–H_2O_2 system, whereas the reaction with I_2–Bu^{t}OOH affords hydroperoxidation products in 66 - 89% yields, iodine being not involved in the target product.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on Bruker AMX-III 400 (400.1 and 100.6 MHz, respectively) and Bruker AVANCE II 300 (300.1 and 75.5 MHz, respectively) spectrometers in $CDCl_3$. Assignments of ^{1}H and ^{13}C signals were made and the structures of the compounds were determinhed with the aid of 2D COSY, NOESY, editing-HSQC, HSQC-TOCSY, and HMBC spectra in the case of studying mixtures **7a**, **8a**, **9a** and **7b**, **8b**.

MeCN (HPLC grade) for ESI-HRMS experiments was ordered from Merck and used as supplied. All samples for ESI-HRMS experiments were prepared in 1.5 mL Eppendorf tubes. All plastic disposables (Eppendorf tubes and tips) used in sample preparation were washed with MeCN before use.

High resolution mass spectra were recorded on a Bruker maXis instrument equipped with electrospray ionization (ESI) ion source.[47,48] The all measurements were performed in a positive (+MS) ion mode (interface capillary voltage: 4500 V) with scan range *m*/*z*: 50 - 3000. External calibration of the mass spectrometer was performed with Electrospray Calibrant Solution (Fluka). A direct syringe injection was used for the all analyzed solutions in MeCN (flow rate: 3 μL/min). Nitrogen was used as nebulizer gas (0.4 bar) and dry gas (4.0 L/min); interface temperature was set at 180 ºC. The all spectra were processed by using Bruker DataAnalysis 4.0 software package.

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 (0.060-0.200 mm, 60 A, CAS 7631-86-9).

Petroleum ether 40-70 (PE), Et_2O, CH_3CN, CH_2Cl_2, and ethyl acetate (EA) were distilled before use over the corresponding drying agents. The reagents I_2, $Na_2S_2O_3$•$5H_2O$, and Na_2SO_4 were of

chemical purity grade. *tert*-Butyl hydroperoxide (70% solution in water), 3,4-dihydro-2*H*-pyran and 2,3-dihydrofuran were purchased from Acros. Bicyclic enol ethers **10a-c** were synthesized according to known procedures.[49,50]

A solution of H_2O_2 was prepared by the extraction with diethyl ether from a 37% aqueous H_2O_2 solution followed by drying over $MgSO_4$.[22] A 51% ethereal solution of *tert*-butyl hydroperoxide was prepared by a similar procedure using tert-Butyl hydroperoxide (70% solution in water).

2,3,4,5,6,7-Hexahydrocyclopenta[*b*]pyran (10a) [49]
Colorless oil.
δ_H (300 MHz, $CDCl_3$): 1.52-2.29 (10 H, m, C(CH_2)$_3$C, C(CH_2)$_2$CH_2O), 3.96 (2H, m, CH_2O).
δ_C (50 MHz, $CDCl_3$): 19.3, 21.8 (CC$H_2$$CH_2CH_2$C), 22.7 (OC$H_2CH_2$$CH_2$C), 30.9 (C$CH_2$(C$H_2$)$_2$C), 32.3 (OC$CH_2$(C$H_2$)$_2$C), 69.8 (O$CH_2$), 106.8 (C$H_2$$CCH_2$), 151.0 (O$CCH_2$).
Calculated (%): C 77.38; H, 9.74 %; Found (%): C, 77.45; H, 9.73. $C_8H_{12}O$.

3,4,5,6,7,8-Hexahydro-2*H*-chromene (10b) [50]
Colorless oil.
δ_H (300 MHz, $CDCl_3$): 1.45-2.34 (12H, m, C(CH_2)$_4$C, (CH_2)$_2$CH_2O), 3.91 (2H, m, CH_2O).
δ_C (50 MHz, $CDCl_3$): 22.9 (OC$H_2$$CH_2$), 23.1 ($CH_2CCH_2CH_2$), 23.26 (C(C$H_2$)$_2CH_2CH_2$C), 25.2 (OC$H_2CH_2$$CH_2$), 27.2 (C$CH_2$(C$H_2$)$_3$C), 28.9 (OC$CH_2$), 65.5 (O$CH_2$), 104.3 (C$H_2$$CCH_2$), 146.7 (O$CCH_2$).
Calculated (%):C, 78.21; H, 10.21; Found (%): C, 78.25; H, 10.18. $C_9H_{14}O$.

2,3,4,5,6,7,8,9-Octahydrocyclohepta[*b*]pyran (10c)
Colorless oil.
δ_H (300 MHz, $CDCl_3$): 1.33-2.45 (14H, m, (CH_2)$_5$, (CH_2)$_2$CH_2O), 3.83 (2H, m, CH_2O).
δ_C (75 MHz, $CDCl_3$): 23.4 (CH_2CH_2O), 25.8 ((CH_2)$_2$$CH_2$(C$H_2$)$_2$), 27.0 (C$H_2$$CH_2$(C$H_2$)$_3$), 27.2 (O(C$H_2$)$_2$$CH_2$), 31.0 (C$H_2$$CCH_2$), 32.5 (OC$CH_2$$CH_2$), 33.2 (OC$CH_2$), 65.4 (O$CH_2$), 108.3 ($CH_2$$CCH_2$), 152.2 (O$CCH_2$).
Calculated (%): C, 78.90; H, 10.59; Found (%): C, 78.96; H, 10.52; $C_{10}H_{16}O$.

Reaction of monocyclic enol ethers 4a,b with the I_2-H_2O_2 system. Synthesis of 7a, 8a, 9a and 7b, 8b.

Iodine (0.256-1.024 g, 1-4 mmol) was dissolved in Et_2O or CH_3CN (10 mL), a 2.53 M ethereal solution H_2O_2 (3.16 mL, 8 mmol) was added, and then a solution of **4a** or **4b** (0.140 or 0.160 g, 2 mmol) in Et_2O (2 mL) was added dropwise with stirring at 0 °C. The mixture was stirred for 30 min at 0 °C. Petroleum ether (20 mL) and finely dispersed $Na_2S_2O_3$•$5H_2O$ (1.5 g) were added, and the mixture was stirred until the it became colorless. The solid residue and possible polymeric resins were separated using a silica gel layer. The solvents were rotary evaporated at 10-15 mmHg and 15-20 °C. The resulting oil (0.420 g for **7-9a** or 0.462 g for **7-8b**) was studied by NMR spectroscopy, including homo- and heteronuclear correlation spectroscopic techniques (COSY, NOESY, editing-HSQC, HSQC-TOCSY and HMBC); the structures of the compounds and their yields were determined from the NMR data.

Experiment to Table 1. Reactions of 3,4-dihydro-2*H*-pyran 4a and 2,3-dihydrofuran 4b with the I_2 – *tert*-butyl hydroperoxide and I_2 – tetrahydropyranyl hydroperoxide systems; synthesis of peroxides 5a,b and 6a,b.

Iodine (0.256-1.024 g, 1-4 mmol) was dissolved in Et_2O or CH_3CN (10 ml), a 51% ethereal solution of *tert*-butyl hydroperoxide (0.693 g, 4 mmol or 1.386 g, 8 mmol) or tetrahydropyranyl hydroperoxide (0.945 g, 8 mmol) was added, and then a solution of **4a** or **4b** (0.14 or 0.16 g, 2 mmol) in Et_2O (2 mL) was added dropwise with stirring at 0 °C. The mixture was stirred for 30 or 120 min at 0 °C (in entry 11, at 20-25°C). Then petroleum ether (20 mL) and finely dispersed $Na_2S_2O_3$•$5H_2O$ (1.5 g) were added, and the mixture was stirred until it became colorless. The solid residue was filtered off. The solvents were rotary evaporated at 10-15 mmHg and 15-20 °C. Peroxides **5a,b** and **6a,b** were isolated from the residue by column chromatography on silica gel. Eluent EA : PE = 1 : 30.

Experiment to Table 2. Reaction of bicyclic enol ethers 10b,c with the I_2-H_2O_2 system to form iodohydroperoxides 11b,c.

Iodine (0.508 g, 2 mmol) was dissolved in Et_2O or CH_3CN (10 ml), a 2.53 M ethereal solution of H_2O_2 (3.16 mL, 8 mmol) was added, and then a solution of enol ether **10** (**10b**, 0.280 g, 2 mmol; **10c**, 0.304 g, 2 mmol) in Et_2O (2 mL) was added dropwise with stirring at 20, 0, or -40 °C. The mixture was stirred for 1 h; in the experiments using cooling, the temperature was gradually raised to 20-25 °C. Then petroleum ether (20 mL) and finely dispersed $Na_2S_2O_3$•$5H_2O$ (1.5 g) were added, and the mixture was stirred until it became colorless. The solid residue was filtered off. The solvents were rotary evaporated at 10-15 mmHg and 15-20 °C. Iodohydroperoxides **11b,c** were isolated from the residue by column chromatography on silica gel. Eluent EA : PE = 1 : 5.

Experiment to Table 3. Reaction of bicyclic enol ethers 10a-c with the I_2-Bu^{t}OOH system to form peroxides 12a-c.

Iodine (0.508 g, 2 mmol) was dissolved in Et_2O or CH_3CN (10 ml), a 51% ethereal solution of *tert*-butyl hydroperoxide (1.386 g, 8 mmol) was added, and then a solution of enol ether **10** (**10a**, 0.248 g, 2 mmol; **10b**, 0.280 g, 2 mmol; **10c**, 0.304 g, 2 mmol) in Et_2O (2 mL) was added dropwise with stirring at 20, 0, -40, or - 70 °C. The mixture was stirred for 1 h with the temperature being gradually raised to 20-25 °C. Then petroleum ether (20 mL) and finely dispersed $Na_2S_2O_3$•$5H_2O$ (1.5 g) were added, and the mixture was stirred until it became colorless. The solid residue was filtered off. The solvents were rotary evaporated at 10-15 mmHg and 15-20 °C. Iodohydroperoxides **12a-c** were isolated from the residue by column chromatography on silica gel. Eluent EA : PE = 1 : 30.

2-(*tert*-Butylperoxy)-3-iodotetrahydrofuran (5a)
Yellow oil. Rf = 0.84 (EA : PE = 1 : 10)
δ_H (200 MHz, $CDCl_3$): 1.21 (9H, s, (CH_3)$_3$C), 2.15-2.19 (1H, m, *H*CHCHI), 2.47-2.54 (1H, m, HC*H*CHI), 4.02-4.22 (3H, m, CH_2O, C*H*I), 5.74 (1H, m, C*H*O).
δ_C (75 MHz, $CDCl_3$): 19.6 (*C*HI), 26.3 (CH_3), 36.5 ($CH_2$$CH_2$O), 67.9 ($CH_2$O), 81.3 (*C*(CH$_3$)$_3$), 113.4 (*C*HO).
IR (KBr): 2979 (vs), 2933 (s), 2897 (s), 1475 (m), 1455 (m), 1439

(m), 1387 (m), 1364 (vs), 1309 (m), 1286 (m), 1245 (s), 1194 (vs), 1151 (m), 1123 (s), 1087 (vs), 1069 (vs), 1036 (s), 996 (vs), 953 9s), 920 (s), 860 (s), 773 (m), 754 (m) cm^{-1}.
HRMS (ESI) m/z $[M+Na]^+$: calculated for $[C_8H_{15}IO_3Na]^+$: 308.9958. Found: 308.9948.

2-(*tert*-Butylperoxy)-3-iodotetrahydro-2*H*-pyran (5b)
Yellow oil. Rf = 0.15 (EA : PE = 1 : 20)
δ_H (300 MHz, $CDCl_3$): 1.28 (9H, s, $(CH_3)_3C$), 1.60-1.66 (2H, m, (CH_2CHI), 2.04-2.07 (1H, m, $HCHCH_2O$), 2.31-2.33 (1H, m, $HCHCH_2O$), 3.62 (1H, m, *H*CHO), 3.99-4.2 (2H, m, HC*H*O, C*H*I), 5.02 (1H, m, C*H*O).
δ_C (75 MHz, $CDCl_3$): 23.4 (*C*HI), 26.4 (CH_2CH_2O), 26.5 (CH_3), 34.6 (CH_2CHI), 64.5 (CH_2O), 81.7 ($C(CH_3)_3$), 104.6 (*C*HO).
IR (KBr): 2977 (vs), (vs), 2865 (s), 1467 (m), 1439 (m), 1387 (m), 1364 (vs), 1259 (m), 1244 (m), 1196 (vs), 1170 (m), 1120 (vs), 1097 (s), 1076 (vs), 1038 (s), 1026 (s), 965 (s), 902 (m), 867 (m), 696 (m), 466 (m) cm^{-1}.
HRMS (ESI) m/z $[M+Na]^+$: calculated for: $[C_9H_{17}IO_3Na]^+$: 323.0115. Found: 323.0120.

2-[(3-Iodotetrahydrofuran-2-yl)peroxy]tetrahydro-2*H*-pyran (6a)
Colorless oil. Rf = 0.6 (EA : PE = 1 : 5)
δ_H (300 MHz, $CDCl_3$): 1.45-2.59 (8H, m, $CHIC\mathit{H}_2$, $(C\mathit{H}_2)_3CH(O)OO$), 3.50-3.65, 3.96-4.25, 5.1-5.25, 5.84-5.91 (7H, m, $2C\mathit{H}_2O$, C*H*I, 2C*H*).
δ_C (75 MHz, $CDCl_3$): 19.0, 19.2, 19.3, 19.9 (CHI, $C\mathit{H}_2(CH_2)_2O$), 25.0 ($C\mathit{H}_2CH_2O$), 27.5, 27.7, 27.8 ($C\mathit{H}_2CH(O)OO$), 36.1, 36.3 ($CHIC\mathit{H}_2$), 62.0, 62.3, 62.4, $(CH_2)_3C\mathit{H}_2O$), 67.8, 68.1 ($CHICH_2C\mathit{H}_2$), 100.2, 100.9, 101.8 ($CH_2C\mathit{H}(O)OO$), 113.2, 113.9 ($CHIC\mathit{H}(O)OO$).
IR (KBr): 2944 (vs), 2895 (s), 2872 (s), 2852 (s), 1469 (m), 1454 (m), 1441 (m), 1352 (m), 1260 (m), 1204 (s), 1186 (m), 1107 (vs), 1085 (s), 1040 (vs), 1017 (s), 983 (s), 955 (vs), 903 (vs), 874 (s), 817 (m), 430 (m) cm^{-1}.
HRMS (ESI) m/z $[M+Na]^+$: calculated for $[C_9H_{15}IO_4Na]^+$: 336.9907. Found: 336.9905.

3-Iodo-2-(tetrahydro-2*H*-pyran-2-ylperoxy)tetrahydro-2*H*-pyran (6b)
Colorless oil. Rf = 0.6 (EA : PE = 1 : 5)
δ_H (300 MHz, $CDCl_3$): 1.52-2.29 (10H, m, $CHIC\mathit{H}_2$, $(C\mathit{H}_2)_3CH(O)OO$), 3.50-3.65, 3.88-4.18, 5.19-5.33 (7H, m, $2C\mathit{H}_2O$, C*H*I, 2C*H*).
δ_C (75 MHz, $CDCl_3$): 19.1, 19.3, 19.5 (*C*HI, $CH_2C\mathit{H}_2(CH_2)_2O$), 24.8, 25.0, 25.1 ($CHICH_2C\mathit{H}_2CH_2O$, $CHOO(CH_2)_2C\mathit{H}_2$), 27.5, 27.6, 27.8 ($C\mathit{H}_2CH(O)OO$), 32.5, 32.7 ($CHOOC\mathit{H}_2$, $CHIC\mathit{H}_2$), 62.0, 62.3, 63.5 ($(CH_2)_3C\mathit{H}_2O$, $CHI(CH_2)_2C\mathit{H}_2O$, $(CH_2)_3C\mathit{H}_2O$), 100.1, 100.3, 101.9 ($CH_2C\mathit{H}(O)OO$), 101.7, 102.0 ($CHIC\mathit{H}(O)OO$).
IR (KBr): 2942 (vs), 2872 (vs), 2852 (vs), 2740 (m), 1737 (m), 1468 (s), 1454 (s), 1441 (vs), 1388 (s), 1352 (vs), 1310 (s), 1283 (s), 1261 (s), 1204 (vs), 1186 (vs), 1106 (vs), 1078 (vs), 1040 (vs), 1017 (vs), 953 (vs), 903 (vs), 874 (vs), 817 (s), 697 (m), 589 (m), 567 (m), 532 (m), 505 (w), 430 (s) cm^{-1}.
HRMS (ESI) m/z $[M+Na]^+$: calculated for $[C_{10}H_{17}IO_4Na]^+$: 351.0064. Found: 351.0062.

4a-Iodooctahydro-8a*H*-chromen-8a-yl hydroperoxide (11b)
White crystals; mp 79-81 °C. Rf = 0.55 (EA : PE = 1 : 5)
δ_H (300 MHz, $CDCl_3$): 1.15-2.70 (12H, m, $(C\mathit{H}_2)_4$, $(C\mathit{H}_2)_2CH_2O$), 3.61-4.05 (2H, m, $C\mathit{H}_2O$), 7.60 (1H, br. s, OO*H*).
δ_C (50 MHz, $CDCl_3$): 22.0, 24.0, 24.6, 30.8, 36.6, 41.1 ($(CH_2)_4$, $(CH_2)_2CH_2O$), 61.5 (CH_2O), 65.1 (*C*-I), 103.8 (COOH).
IR (KBr): 3459 (vs), 3264 (vs), 2955 (vs), 2938 (vs), 2887 (s), 2863 (s), 1712 (m), 1460 (s), 1367 (s), 1289 (s), 1217 (vs), 1190 (vs), 1165 (s), 1094 (s), 1054 (vs), 987 (vs), 902 (s), 869 (s), 842 (m), 799 (m), 727 (m), 604 (m), 550 (s), 476 (m) cm^{-1}.
HRMS (ESI) m/z $[M-OOH]^+$: calculated for $[C_9H_{14}IO]^+$: 265.0084. Found: 265.0093.

4a-Iodooctahydrocyclohepta[*b*]pyran-9a(2*H*)-yl hydroperoxide (11c)
Yellow oil. Rf = 0.39 (EA : PE = 1 : 5)
δ_H (300 MHz, $CDCl_3$): 1.15-2.50 (14H, m, $(C\mathit{H}_2)_5$, $(C\mathit{H}_2)_2CH_2O$), 3.50-3.80 (2H, m, $C\mathit{H}_2O$).
δ_C (75 MHz, $CDCl_3$): 20.7, 21.0, 25.8, 27.6, 33.8, 36.4, 44.9 ($(CH_2)_5$, $(CH_2)_2CH_2O$), 61.1 (CH_2O), 61.5 (CI), 106.3 (COOH).
IR (KBr): 3355 (m), 2930 (vs), 2860 (s), 1705 (m), 1450 (m), 1359 (m), 1212 (m), 1074 (s), 996 (m), 892 (m), 732 (m) cm^{-1}.
HRMS (ESI) m/z $[M+Na-HI]^+$: calculated for $[C_{10}H_{16}O_3]^+$: 207.0992. Found: 207.1009.

7a-(*tert*-Butylperoxy)octahydrocyclopenta[*b*]pyran (12a)
Yellow oil. Rf = 0.12 (EA : PE = 1 : 10)
δ_H (300 MHz, $CDCl_3$): 1.23-2.14 (20H, m, $(C\mathit{H}_2)_3COO$, $(C\mathit{H}_2)_2CH(CH_2)_3$, CH), 3.66-3.87 (2H, m, CH_2O).
δ_C (50 MHz, $CDCl_3$): 21.0 ($CHCH_2C\mathit{H}_2CH_2C$), 22.8 ($C\mathit{H}_2CH_2O$), 26.7 ($C(C\mathit{H}_3)_3$), 28.5, 31.2 ($CHC\mathit{H}_2CH_2$, $CH_2C\mathit{H}_2CH$), 36.0 ($CC\mathit{H}_2$), 39.5 (CH), 61.0 (CH_2O), 79.0 ($OOC(CH_3)_3$), 110.1 (OCOO).
IR (KBr): 3424 (m), 2944 (vs), 2878 (s), 1738 (s), 1464 (m), 1446 (m), 1067 (s), 993 (s), 915 (m), 900 (m) cm^{-1}.
HRMS (ESI) m/z $[M]^+$: calculated for $[C_{12}H_{21}O_3]^+$: 213.1485. Found: 213.1492.

8a-(*tert*-Butylperoxy)octahydro-2*H*-chromene (12b)
Yellow oil. Rf = 0.11 (EA : PE = 1 : 10)
δ_H (300 MHz, $CDCl_3$): 1.21-1.54 (22H, m, $C(C\mathit{H}_2)_4C$, $(C\mathit{H}_3)_3C$, $OCH_2(C\mathit{H}_2)_2CH$, CH), 3.64-3.98 (2H, m, $C\mathit{H}_2O$).
δ_C (50 MHz, $CDCl_3$): 22.5, 25.9 ($CCH_2C\mathit{H}_2(CH_2)_2CH$, $OCH_2C\mathit{H}_2$), 26.3, 26.6 ($CHCH_2C\mathit{H}_2(CH_2)_2)C$, $CH(CH_2)_2C\mathit{H}_2CH_2CH$), 26.8 ($C(C\mathit{H}_3)_3$) 29.8 ($CHC\mathit{H}_2$), 32.3 ($OOCC\mathit{H}_2$) 44.6 (CH), 60.9 ($CH_2O$), 78.8 ($OOC(CH_3)_3$), 101.3 (OCOO).
IR (KBr): 2977 (vs), 2936 (vs), 2883 (s), 2860 (s), 1447 (m), 1362 (s), 1254 (m), 1243 (m), 1214 (m), 1200 (s), 1107 (m), 1091 (vs), 1025 (m), 994 (m), 969 (m), 957 (m), 931 (s), 892 (m), 867 (m), cm^{-1}.
HRMS (ESI) m/z $[M+Na]^+$: calculated for $[C_{13}H_{24}O_3Na]^+$: 251.1618. Found: 251.1619.

9a-(*tert*-Butylperoxy)decahydrocyclohepta[*b*]pyran (12c)
Yellow oil. Rf = 0.14 (EA : PE = 1 : 10)
δ_H (300 MHz, $CDCl_3$): 1.20-2.01 (24H, m, $C(C\mathit{H}_2)_5C$, $(C\mathit{H}_3)_3C$, $OCH_2(C\mathit{H}_2)_2C$, CH), 3.59-4.10 (2H, m, $C\mathit{H}_2O$).
δ_C (50 MHz, $CDCl_3$): 20.7, 21.5, 23.4, 26.1 ($C(CH_2)_2C\mathit{H}_2(CH_2)_2C$, $CH_2C\mathit{H}_2(CH_2)_3$, $OCCH_2C\mathit{H}_2(CH_2)_3C$, $OCH_2C\mathit{H}_2$), 26.7 ($C(C\mathit{H}_3)_3$) 29.8 ($CHC\mathit{H}_2$), 31.4 ($O(CH_2)_2C\mathit{H}_2CH$), 34.4 ($OCC\mathit{H}_2$), 38.3 (CH),

62.4 (CH_2O), 78.7 ($OOC(CH_3)_3$), 105.7 (OCOO).
IR (KBr): 3400 (m), 2974 (vs), 2934 (vs), 2864 (s), 1735 (s), 1704 (vs), 1456 (m), 1363 (s), 1243 (s), 1197 (s), 1170 (m), 1154 (m), 1052 (m), 910 (m) cm^{-1}.
HRMS (ESI) m/z $[M+Na]^+$: calculated for $[C_{14}H_{26}O_3Na]^+$: 265.1774. Found: 265.1773.

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Notes and references

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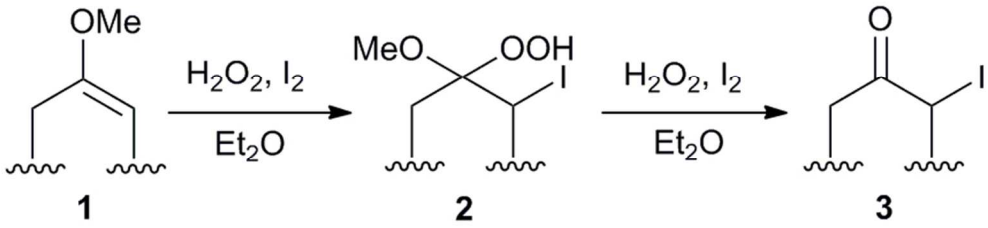

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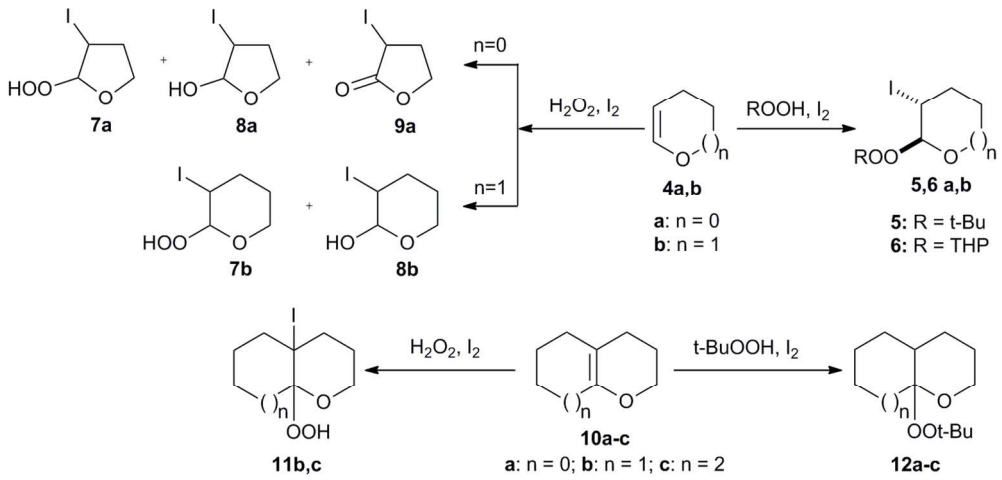

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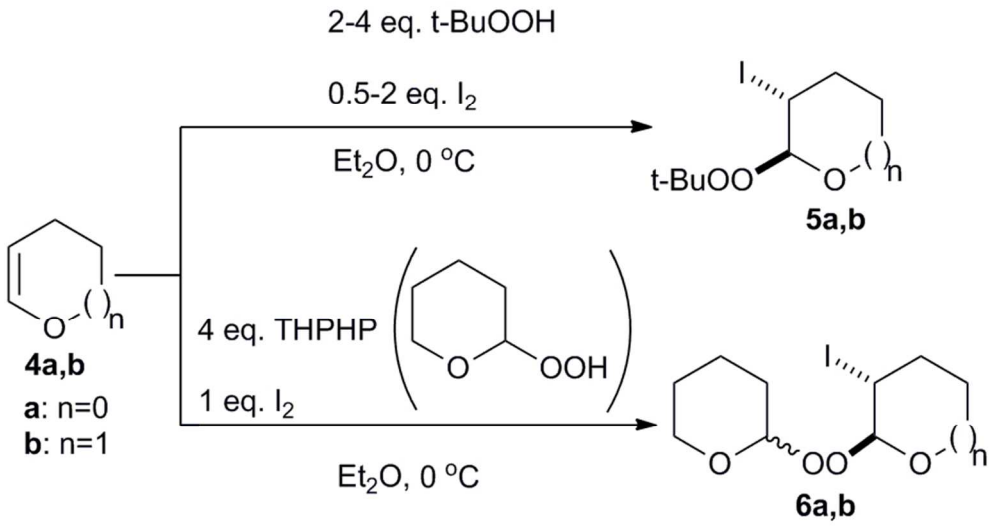

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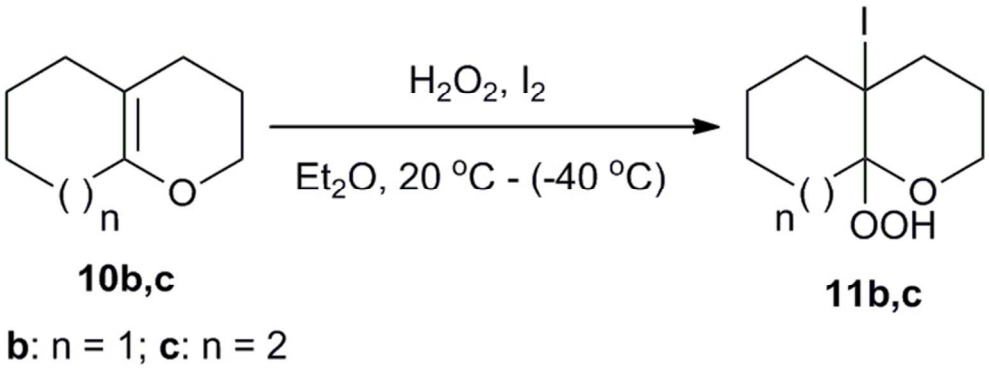

10b,c **11b,c**

b: n = 1; **c**: n = 2

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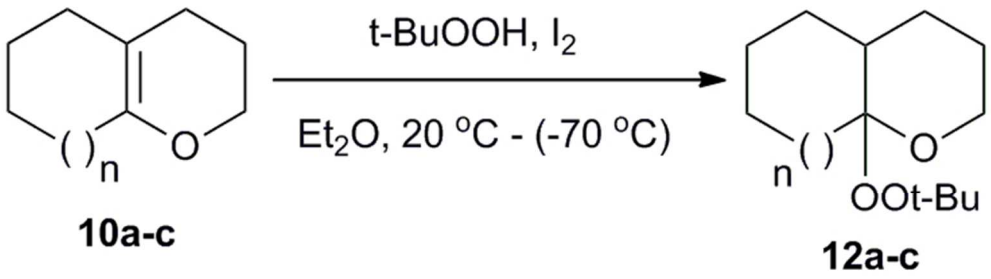

10a-c **12a-c**

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