SYNTHESIS OF 3-HYDROPEROXY (OR HYDROXY)-
SUBSTITUTED 1,2-DIOXANES AND 1,2-DIOXEPANES BY
THE OZONOLYSIS OF UNSATURATED HYDROPEROXY
ACETALS

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Abstract - Mono-ozonolysis of dienes in methanol gave in each case the
corresponding unsaturated hydroperoxy acetal. The reaction of the
hydroperoxides with ozone in the solvent system such as AcOH-CH₂Cl₂
resulted in the production of the corresponding hydroperoxy (or hydroxy)-
substituted 1,2-dioxanes or 1,2-dioxepanes in good yield. By the treatment of
the derived products with TMSOTf-Et₃SiH, replacement of the methoxy (or
hydroxy) group by hydrogen was accomplished.

The discovery of pharmacologically active six- and seven-membered ring peroxides has placed a renewed
interest for the development of new synthetic methods of cyclic peroxides having these structures.¹ In this
respect, we² and Dussault³ reported independently that the ozonolysis or the halonium ion-mediated
cyclization of unsaturated hydroperoxy acetals, derived from capture of carbonyl oxide intermediates by
unsaturated alcohols, are convenient methods for the synthesis of 1,2,4-trioxanes and 1,2,4-trioxepanes.
Since 1,2-dioxane derivatives such as arteflene and yingzhaosu C are also known to show remarkable
antimalarial activities,⁴⁻⁶ we have examined the ozonolysis of the unsaturated hydroperoxy acetals, derived
from trapping of unsaturated carbonyl oxides by methanol and have found that the reaction in the solvent
system such as AcOH-CH₂Cl₂ is quite useful for the synthesis of the hydroperoxy (or hydroxy)-
substituted 1,2-dioxanes and 1,2-dioxepanes. As an alternative way for the synthesis of the target
compounds, the reaction of unsaturated ketones in methanol has been also examined.
RESULTS AND DISCUSSION

Preparation of Unsaturated Hydroperoxy Acetals
As reported before, the preparation of unsaturated hydroperoxy acetals was conducted by the sequence illustrated in Scheme 1. The hydroperoxide (3a) obtained from the ozonolysis of 2a in methanol was a single isomer, suggesting that capture of the 2-alkyl-substituted cyclohexanone O-oxide by methanol occurs from the less hindered face. The unsaturated hydroperoxy acetals (3c, f) were also isolated as the single isomers (Schemes 3 and 5). In the case of the hydroperoxide (3b'), 2-methoxyethanol was used as the trapping agent of the carbonyl oxide intermediate (Scheme 2).

Ozonolysis of Unsaturated Hydroperoxy Acetals
We conducted first the ozonolysis of the hydroperoxide (3a) in ether. The product was the dioxane (6a) (71%; a single isomer) (Scheme 2). No evidence was obtained for the formation of the ozonide (7a), derived from an intermolecular [3 + 2] cycloaddition of the carbonyl oxide intermediate (5a) with formaldehyde. In other words, the formation of the entropically favored dioxane is very fast. The reaction in AcOH-CH₂Cl₂ also gave the dioxane (6a) in moderate yield. The NOE measurement of 6a suggested

![Scheme 1](attachment://Scheme_1.png)

![Scheme 2](attachment://Scheme_2.png)
that the hydroperoxy group is cis with both the methoxy group and the bridgehead hydrogen. From the hydroperoxide (3b'), the dioxane (6b') was obtained in 54% yield (a 3:2 mixture of two isomers). Ozonolysis of the unsaturated hydroperoxide (3c) gave the hydroxy-substituted dioxane (9c) was the sole product (57%; a 3:2 mixture of two isomers) (Scheme 3). This is in marked contrast to the fact that only the hydroperoxy-substituted 1,2-dioxane (6a) was produced from the hydroperoxide (3a). This remarkable difference in behavior between two hydroperoxides (3a) and (3c) is rationalized in terms of the directive effect of the electron-donating methyl substituents on the cleavage of the primary ozonides (4a) and (4c). Thus, the reaction of 3a proceeds by the carbonyl oxide intermediate (5a), thereby providing the hydroperoxy-substituted 1,2-dioxane (6a) (Scheme 2). In the case of the primary ozonide (4c), however, the alternative mode of the cleavage yielding the keto hydroperoxide (8c) predominates and as a result, the hydroxy-substituted 1,2-dioxane (9c) is exclusively produced (Scheme 3). Since the 1H NMR spectrum of the mixture of 9c was quite complex, we failed to determine the stereochemistry.

The hydroperoxide (3d) seems to be a borderline case (Scheme 3). The ozonolysis of the hydroperoxide
(3d) in AcOH-CH₂Cl₂ gave only a complex mixture of unidentified products. When the same reaction was repeated in a less acidic solvent system, trifluoroethanol (TFE)-CH₂Cl₂, however, both the hydroperoxy- and hydroxy-substituted 1,2-dioxanes (6d) and (9d) were certainly obtained in yields of 20% and 31%, respectively (Scheme 3). The formation of both 6d and 9d implies that in the case of the primary ozonide (4d) two fission pathways contribute to a similar extent. Consistent with this, the reaction of 3d in ether resulted in the formation of the ozonide (7d) (24%) together with the hydroxy-substituted 1,2-dioxane (9d) (24%). The 1,2-dioxane (6d) was found to be labile not only in a solvent such as CDCl₃ but also in the solid state; even in a refrigerator it decomposed into the unidentified products in less than one week. Thus, the stereochemistry of 6d, although isolated as a single isomer, could not be determined. The same trend was observed for 9d.

In connection with the easy formation of the hydroxy-substituted 1,2-dioxane (9d) from 3d, it is well known that the \( \gamma \)-hydroperoxy-substituted ketones, if formed, are immediately transformed to the corresponding hydroxy-substituted 1,2-dioxanes by cyclization. \(^{5a,b,g}\) Therefore, we then conducted the ozonolysis of the unsaturated ketones (1a,c)\(^1\) in MeOH-CH₂Cl₂. Ozonolysis of 1a gave, together with the ozonide (12a) (24%), the hydroxy-substituted 1,2-dioxane (13a) in 57% yield (a 3:1 mixture of two isomers which could be separated by column chromatography on silica gel) (Scheme 4). Because of the complex overlapping of the signals in \(^1\)H NMR spectrum, we failed to determine the structure of the major isomer of 13a by the HH, CH COSY and NOE measurements. In contrast to the reaction of 1a, the reaction of the unsaturated ketone (1c) provided only the corresponding keto aldehyde (14c). These results demonstrate that in the ozonolysis of the keto olefins (1a,c) also, the substituent-dependent selectivity in cleavage of the primary ozonides is important in determining the structure of the products.

We next examined the synthesis of the 1,2-dioepane derivatives from the hydroperoxides (3e,f) with a longer tether (Scheme 5). By the ozonolysis of the hydroperoxide (3e) in AcOH-CH₂Cl₂, the keto hydroperoxide (8e) (36%) was obtained together with the expected dioepane (6e) (30% yield). In
contrast, the ozonolysis of the hydroperoxide (3f) gave only the corresponding dioxepane (6f) (55% yield; a 3:2 mixture of two isomers). It is interesting to note that the keto hydroperoxide (8e) did not cyclize to the corresponding dioxepane; ozonolysis of 1e in methanol has been found to give 8e in 90% yield. In the case of the keto olefin (1f), however, treatment with ozone in methanol resulted in the formation of the hydroxy-substituted 1,2-dioxepane (13f) (70%; a 3:1 mixture of two isomers) together with the ozonide 12f (7%). The remarkable difference in behavior between 8e and 11f demonstrates that the factor of entropy is important for the efficiency of cyclization of keto hydroperoxides.

Reduction of 3-Hydroperoxy (or Hydroxy)-Substituted 1,2-Dioxanes and 1,2-Dioxepanes with TMSOTf-Et$_3$SiH

We next examined the possibility of transformation of the hydroperoxy (or hydroxy)-substituted 1,2-dioxane and dioxepane (Scheme 6). Treatment of 13a with TMSOTf-Et$_3$SiH$^{11}$ gave the expected dioxane (15a) (39%; a single isomer). All our trial to determine the stereochemistry of 15a by NMR
spectroscopy failed, because the signals overlapped in a complicated fashion. The reaction of the ozonide (12a) under the same conditions, however, resulted in the formation of the corresponding tetrahydrofuran (16a) (51%; a single isomer). A possible mechanism of the transformation is illustrated in Scheme 6. In the case of the ozonide (12a), TMSOTf seems to induce cleavage of the C-O bond of the peroxide bridge rather than the ether bridge. Surprisingly, treatment of 13f with a mixture of TMSOTf and Et₃SiH gave the novel tricyclic peroxide containing a 1,2,4-trioxolane structure in a high yield of 82%, suggesting that the intramolecular cyclization leading to 12f is much faster than the hydride ion transfer from Et₃SiH to the carbocation center of 17f. In contrast, treatment of the iodomethyl-substituted dioxepane (20), obtained from 3f by the I⁺-mediated cyclization, with TMSOTf/Et₃SiH gave the expected dioxepane derivative (21) (56%). From 18, the dioxane (19) was obtained in 59% yield (Scheme 6).

**Scheme 6**

![Scheme 6](image)

**EXPERIMENTAL**

¹H (270 MHz) and ¹³C NMR (67.5 MHz) spectra were obtained in CDCl₃ with SiMe₄ as standard. The method of ozonolysis was previously described.¹⁵

**Caution:** Since organic peroxides are potentially hazardous compounds, they must be handled with due care; avoid exposure to strong heat or light, or mechanical shock, or oxidizable organic materials, or transition metal ions.

**Mono-ozonolysis of Dienes in MeOH-CH₂Cl₂**
Ozonolysis of the vinyl ether (2b) is representative. To a solution of 2b (340 mg, 2.5 mmol) in CH$_2$Cl$_2$ (25 mL) and 2-methoxyethanol (5 mL) was passed a slow stream of ozone (1 equiv.) at -70 °C. After adding ether (70 mL), the organic layer was washed with ice-cold 10% sodium bicarbonate, saturated brine, and dried over anhydrous MgSO$_4$. After evaporation of the solvent under vacuum, the residue was separated by column chromatography on silica gel. Elution with ether-hexane (12:88) gave the unsaturated hydroperoxide (3b') (51 mg, 10%).

2-(2-Methoxyethoxy)-5-methyl-5-hexen-2-yl hydroperoxide (3b')
A colorless oil, $^1$H NMR δ 1.34 (s, 3 H), 1.7-2.2 (m, 4 H), 1.72 (s, 3 H), 3.34 (s, 3 H), 3.57 (t, $J = 4.3$ Hz, 2 H), 3.72 (t, $J = 4.3$ Hz, 2 H), 4.69 (s, 2 H), 10.27 (s, 1 H); $^{13}$C NMR δ 19.70, 22.64, 32.15, 33.52, 58.92, 59.86, 72.89, 106.96, 109.65, 145.34.

Ozonolysis of Unsaturated Hydroperoxy Acetals (3a,b',c-f) in AcOH-CH$_2$Cl$_2$
The reaction of the hydroperoxide (3a) is representative. A solution of 3a (260 mg, 1.3 mmol) in acetic acid (5 mL)-CH$_2$Cl$_2$ (25 mL) was cooled to -70 °C, and ozone (1.5 equiv.) was bubbled through it at -70 °C. Aqueous 10% NaHCO$_3$ was added, and the mixture was extracted with ether (70 mL), washed with saturated brine, and dried over anhydrous MgSO$_4$. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether-hexane (1:9) gave the hydroperoxy-substituted 1,2-dioxane (6a) (200 mg, 71%).

1-Methoxy-4-methyl-2,3-dioxabicyclo[4.4.0]decan-4-yl hydroperoxide (6a)
A colorless oil, $^1$H NMR δ 1.2-1.8 (m, 10 H), 1.8-1.9 (m, 1 H), 1.42 (s, 3 H), 3.29 (s, 3 H), 8.90 (s, 1 H); $^{13}$C NMR δ 19.50, 21.76, 22.52, 27.10, 27.82, 32.92, 48.47, 104.21, 109.04. Anal. Calcd for C$_{10}$H$_{18}$O$_5$: C, 55.03; H, 8.31. Found: C, 54.58; H, 8.17. Irradiation of the methoxy proton resulted in the small enhancement of the signals of the OOH and the hydrogen at C-6 [δ 1.8-1.9 (m)]. No enhancement of the methyl signal [δ 1.42 (s)] was observed by the irradiation.

6-(2-Methoxyethoxy)-3,6-dimethyl-1,2-dioxan-3-yl hydroperoxide (6b')
A colorless oil (a 3:2 mixture of two isomers), $^1$H NMR δ 1.31 (s, major) + 1.43 (s) + 1.44 (s, major) + 1.48 (s) (6 H), 1.5-2.2 (m, 4 H), 3.38 (s) + 3.40 (s, major) + 3.4-3.8 (m, 4 H), 8.36 (s, major) + 9.04 (s) (1 H); $^{13}$C NMR δ 19.70, 19.89, 20.16, 20.43, 26.38, 27.53, 29.53, 30.98, 58.94, 59.01, 60.72, 61.13, 71.92 (2C), 102.41, 102.97, 106.92, 107.35. Anal. Calcd for C$_9$H$_{18}$O$_6$: C, 48.64; H, 8.16. Found: C, 48.85; H, 8.17.

4-Hydroxy-1-methoxy-2,3-dioxabicyclo[4.4.0]decan (9c)
A colorless oil (a 3:2 mixture of two isomers), $^1$H NMR δ 1.1-2.2 (m, 11 H), 3.33 (s, 3 H), 3.57 (d, $J = 3.9$ Hz, major) + 3.87 (d, $J = 7.3$ Hz) (1 H), 5.3-5.4 (m, 1 H); $^{13}$C NMR δ 21.96 (CH$_2$), 22.73 (CH$_2$), 24.28 (CH$_3$), 27.42 (CH$_3$), 28.16 (CH$_3$), 28.70 (CH$_3$), 29.87 (CH$_3$), 30.87 (CH$_3$), 32.85 (CH$_3$), 34.25 (CH), 37.61 (CH), 48.23 (CH$_3$), 48.57 (CH$_3$), 94.30 (CH), 97.40 (CH), 101.58 (C), 104.65 (C). Anal. Calcd for C$_9$H$_{16}$O$_3$: C, 57.43; H, 8.57. Found: C, 57.71; H, 8.48.

7-Methoxy-3,7-dimethyl-1,2-dioxepan-3-yl hydroperoxide (6e)
A colorless oil (a 1:1 mixture of two isomers), $^1$H NMR δ 1.26 (s) + 1.41 (s) + 1.43 (s) + 1.47 (s) (6 H), 1.6-2.0 (m, 6 H), 3.34 (s) + 3.35 (s, 3 H), 8.39 (s) + 8.60 (s) (1 H); $^{13}$C NMR δ 18.28 (CH$_2$), 18.58 (CH$_2$), 18.96 (CH$_3$), 19.46 (CH$_3$), 19.70 (CH$_3$), 20.04 (CH$_3$), 35.35 (CH$_2$), 38.87 (CH$_2$), 40.09 (CH$_2$),
49.24 (CH₃), 49.92 (CH₃), 107.60 (C), 108.36 (C), 111.81 (C), 112.47 (C). Anal. Calcd for C₈H₁₆O₅: C, 49.99; H, 8.39. Found: C, 50.03; H, 8.38.

6-Hydroperoxy-6-methoxy-2-heptanone (8e)
A colorless oil, ¹H NMR δ 1.2-2.0 (m, 4 H), 1.24 (s, 3 H), 2.09 (s, 3 H), 2.3-2.5 (m, 2 H), 3.26 (s, 3 H), 8.34 (br s, 1 H); ¹³C NMR δ 17.81, 18.39, 29.92, 42.93, 48.84, 106.56, 209.61. Anal. Calcd for C₈H₁₆O₅: C, 54.53; H, 9.15. Found: C, 54.47; H, 9.32.

1-Methoxy-4-methyl-2,3-dioxabicyclo[5.4.0]undecan-4-yl hydroperoxide (6f)
A colorless oil (a 3:2 mixture of two isomers), ¹H NMR δ 1.2-2.4 (m, 13 H), 1.40 (s, major) + 1.44 (s) (3 H), 3.28 (s) + 3.31 (s, major) (3 H), 8.45 (s) + 8.74 (s, major) (1 H); ¹³C NMR δ 19.52 (CH₃), 19.61 (CH₃), 20.65 (CH₂), 22.21 (CH₂), 22.73 (CH₃), 24.49 (CH₂), 24.57 (CH₂), 24.91 (CH₂), 25.11 (CH₂), 28.97 (CH₂), 30.55 (CH₂), 33.28 (CH₂), 35.06 (CH₂), 39.43 (CH), 48.16 (CH₃), 49.24 (CH₃), 108.12 (C), 109.31 (C), 111.41 (C), 112.17 (C). Anal. Calcd for C₁₁H₂₀O₅: C, 56.88; H, 8.68. Found: C, 56.91; H, 8.62.

Ozonolysis of the Unsaturated Hydroperoxy Acetal (3c) in CF₃CH₂OH-CH₂Cl₂
A solution of 3d (230 mg, 0.81 mmol) in trifluoroethanol (TFE)-CH₂Cl₂ (1:2 v/v; 25 mL) was cooled to 0 °C, and ozone (1.5 equiv.) was bubbled through it at 0 °C. Aqueous 10% NaHCO₃ was added, and the mixture was extracted with ether, washed with saturated brine, and dried over anhydrous MgSO₄. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether-hexane (1:9) gave the hydroperoxy-substituted dioxane (6d) (55 mg, 20%). Subsequent elution with ether-hexane (12:88) gave the hydroxy-substituted dioxane (9d) (76 mg, 31%).

4-Methoxy-1,4-diphenyl-2,3-dioxanyl hydroperoxide (6d)
A white powder, mp 152-153 °C (ether-hexane), ¹H NMR δ 1.9-2.3 (m, 4 H), 3.36 (s, 3 H), 7.3-7.6 (m, 10 H), 8.49 (s, 1 H); ¹³C NMR δ 28.77, 31.79, 50.73, 103.99, 108.07, 125.84, 128.46, 128.61, 128.81, 137.84, 138.54. Anal. Calcd for C₁₇H₁₈O₅: C, 67.54; H, 6.00. Found: C, 67.48; H, 5.84.

3-Hydroxy-6-methoxy-3,6-diphenyl-1,2-dioxane (9d)
A white powder, mp 127-128 °C (ether-hexane), ¹H NMR δ 1.9-2.3 (m, 4 H), 3.32 (s, major) + 3.33 (s) (3 H), 5.12 (s, 1 H), 5.20 (s, 1 H), 7.2-7.4 (m, 10 H), 7.9 (br s, 1 H); ¹³C NMR δ 30.60, 31.92, 50.62, 100.05, 102.77, 125.41, 125.73, 126.56, 128.45, 128.54, 128.59, 129.00, 139.33, 141.26. Anal. Calcd for C₁₇H₁₈O₄: C, 71.31; H, 6.34. Found: C, 71.59; H, 5.92.

Ozonolysis of the Unsaturated Hydroperoxy Acetals 3 in Ether
The reaction of 3d is representative. A solution of 3d (250 mg, 1.1 mmol) in ether (30 mL) was cooled to -70 °C, and ozone (1.5 equiv.) was bubbled through it at -70 °C. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether-hexane (1:9) gave the hydroperoxy-substituted dioxane (6d) (55 mg, 20%). Subsequent elution with ether-hexane (12:88) gave the hydroxy-substituted dioxane (9d) (76 mg, 31%).

4-Methoxy-1,4-diphenyl-2,3-dioxanyl hydroperoxide (6d)
A white powder, mp 152-153 °C (ether-hexane), ¹H NMR δ 1.9-2.3 (m, 4 H), 3.36 (s, 3 H), 7.3-7.6 (m, 10 H), 8.49 (s, 1 H); ¹³C NMR δ 28.77, 31.79, 50.73, 103.99, 108.07, 125.84, 128.46, 128.61, 128.81, 137.84, 138.54. Anal. Calcd for C₁₇H₁₈O₅: C, 67.54; H, 6.00. Found: C, 67.48; H, 5.84.

3-Hydroxy-6-methoxy-3,6-diphenyl-1,2-dioxane (9d)
A white powder, mp 127-128 °C (ether-hexane), ¹H NMR δ 1.9-2.3 (m, 4 H), 3.32 (s, 3 H), 7.3-7.7 (m, 10 H); ¹³C NMR δ 30.60, 31.92, 50.62, 100.05, 102.77, 125.41, 125.73, 126.56, 128.45, 128.54, 128.59, 129.00, 139.33, 141.26. Anal. Calcd for C₁₇H₁₈O₄: C, 71.31; H, 6.34. Found: C, 71.59; H, 5.92.

Ozonolysis of the Unsaturated Hydroperoxy Acetals 3 in Ether
The reaction of 3d is representative. A solution of 3d (250 mg, 1.1 mmol) in ether (30 mL) was cooled to -70 °C, and ozone (1.5 equiv.) was bubbled through it at -70 °C. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether-hexane (12:88) gave the hydroxy-substituted dioxane (9d) (85 mg, 24%). Subsequent elution with ether-hexane (16:84) gave the ozonide (7d) (85 mg, 24%).

1-Methoxy-1-phenyl-3-(3-phenyl-1,2,4-trioxolan-3-yl)propyl hydroperoxide (7d)
A white powder (a 2:1 mixture of two isomers), mp 117-124 °C (ethyl acetate), ¹H NMR δ 1.8-2.2 (m, 4 H), 3.22 (s, major) + 3.23 (s) (3 H), 5.12 (s, 1 H), 5.20 (s, 1 H), 7.2-7.4 (m, 10 H), 7.9 (br s, 1 H); ¹³C NMR δ 29.78 (CH₂), 29.83 (CH₂), 31.48 (CH₂), 49.44 (CH₃), 49.49 (CH₃), 94.70 (CH₂), 107.94 (C),
1-Methoxy-2-[(3-methyl-1,2,4-trioxolan-3-yl)ethyl]cyclohexyl hydroperoxide (7f)
An oil; 1H NMR δ 1.5-2.0 (m, 13 H), 1.46 (s, 3 H), 3.31 (s, 3 H), 5.09 (s, 1 H), 5.15 (s, 1 H), 7.96 (s, 1 H). Anal. Calcd for C_{18}H_{20}O_{6}: C, 65.05; H, 6.07. Found: C, 64.82; H, 5.94.

Ozonolysis of the Unsaturated Ketone (1) in Methanol
The reaction of 1a is representative. A solution of 1a (228 mg, 1.5 mmol) in MeOH-CH_2Cl_2 (1:4 v/v; 25 mL) was cooled to -70 °C, and ozone (1.2 equiv.) was bubbled through it at -70 °C. After evaporation of the solvent, the crude products were separated by column chromatography on silica gel. Elution with ether-hexane (1:9) gave the ozonide (12a) (60 mg, 24%). Elution with ether-hexane (14:86) gave the hydroxy-substituted dioxane (13a) (major isomer; 130 mg, 43%). Subsequent elution with ether-hexane (18:82) gave the minor isomer of (13a) (41 mg, 14%).

8-Methyl-9,10,11-trioxatricyclo[6.2.1.0^{1,6}]undecane (12a)
A colorless oil, 1H NMR δ 0.9-2.3 (m, 11 H), 1.67 (s, 3 H); 13C NMR δ 15.09 (CH_3), 23.22 (CH_2), 24.08 (CH_2), 24.76 (CH_2), 32.98 (CH_3), 42.30 (CH), 42.55 (CH_2), 110.89, 110.93. Anal. Calcd for C_9H_{14}O_3: C, 63.51; H, 8.29. Found: C, 63.45; H, 7.96.

1-Hydroxy-4-methoxy-4-methyl-2,3-dioxabicyclo[4.4.0]decane (13a: major isomer)
A white powder, mp 97-98 °C (ether-hexane), 1H NMR δ 1.2-2.2 (m, 11 H), 1.23 (s, 3 H), 2.84 (s, 1 H), 3.28 (s, 3 H); 13C NMR δ 20.83, 23.13, 25.48, 28.00, 33.84, 35.01, 36.28, 49.08, 99.84, 102.64. Anal. Calcd for C_{10}H_{18}O_4: C, 59.39; H, 8.97. Found: C, 59.33; H, 8.92.

1,2-Dioxane (13a) (minor isomer)
A white powder, mp 97-98 °C (ether-hexane), 1H NMR δ 1.2-2.2 (m, 11 H), 1.23 (s, 3 H), 2.84 (s, 1 H), 3.28 (s, 3 H); 13C NMR δ 20.83, 23.13, 25.48, 28.00, 33.84, 35.01, 36.28, 49.08, 99.84, 102.64. Anal. Calcd for C_{10}H_{18}O_4: C, 59.39; H, 8.97. Found: C, 59.24; H, 8.87.

9-Methyl-10,11,12-trioxatricyclo[7.2.1.0^{1,6}]undecane (12f)
An oil; 1H NMR δ 1.2-1.9 (m, 13 H), 1.50 (s, 3 H); 13C NMR δ 21.21, 23.61, 24.08, 24.84, 30.42, 32.42, 34.09, 39.91, 107.94, 109.26. Anal. Calcd for C_{10}H_{16}O_3: C, 65.19; H, 8.75. Found: C, 65.38; H, 8.65.

1-Hydroxy-4-methoxy-4-methyl-2,3-dioxabicyclo[5.4.0]dodecane (13f)
A white powder (a 3:1 mixture of two isomers), mp 76-79 °C (ether-hexane); 1H NMR δ 1.2-2.1 (m, 13 H), 1.27 (s) + 1.30 (s) (3 H), 3.34 (s) + 3.38 (s) (3 H), 3.60 (s) + 3.61 (s) (1 H); 13C NMR δ 22.86, 25.20, 25.57, 30.62, 34.92, 40.61, 49.04, 51.20, 104.33, 107.69. Anal. Calcd for C_{11}H_{20}O_4: C, 61.09; H, 9.32. Found: C, 61.23; H, 9.24.

2-(Formylmethyl)cyclohexanone (14c)
An oil; 1H NMR δ 1.2-2.0 (m, 4 H), 2.0-2.4 (m, 5 H), 2.8-3.0 (m, 2 H), 9.80 (s, 1 H); 13C NMR δ 25.14, 27.66, 33.95, 41.67, 43.54, 45.37, 200.79, 210.82. HRMS [(M + H)^+] m/z Calcd for C_{8}H_{12}O_2 140.0837, Found 140.0838.

Reaction of the Hydroxy-substituted 1,2-Dioxanes with TMSOTf-Et_3SiH
The reaction of \(13a\) is representative. To a solution of \(13a\) (472 mg, 2.3 mmol) in \(\text{CH}_2\text{Cl}_2\) (30 mL) were added \(\text{Et}_3\text{SiH}\) (1.2 g, 10.1 mmol) and then TMSOTf (1.1 g, 5.1 mmol) in 10 min and the mixture was stirred at -70 °C for 1 h under nitrogen atmosphere. The mixture was poured into aqueous 10 % \(\text{NaHCO}_3\) and extracted with ether. The organic layer was washed with saturated brined and dried over anhydrous \(\text{MgSO}_4\). After evaporation of the solvent, the residue was separated by column chromatography on silica gel. Elution with ether-hexane (5:95) gave the 1,2-dioxane (\(15a\)) (141 mg, 39%).

4-Methyl-2,3-dioxabicyclo[4.4.0]decane (\(15a\))

A colorless oil, \(^1\text{H} \text{NMR } \delta 0.9-1.8 \text{ (m, 11 H)}, 1.03 \text{ (d, } J = 6.27 \text{ Hz, 3 H)}, 3.6-3.7 \text{ (m, 1 H)}; \(^{13}\text{C NMR } \delta 18.89 \text{ (CH}_3\text{)}, 24.84 \text{ (CH}_2\text{)}, 25.38 \text{ (CH}_2\text{)}, 28.61 \text{ (CH}_2\text{)}, 30.44 \text{ (CH}_2\text{)}, 38.30 \text{ (CH)_2}, 40.72 \text{ (CH)}; 78.44 \text{ (CH)}; 85.28 \text{ (CH)}; \text{HRMS (M}^+\text{) } m/z \text{ calcd for C}_9\text{H}_{16}\text{O}_2 \text{ 156.1150, Found 156.1167.}

Reactions of the Ozonide (\(12a\)), Dioxane (\(18\)) or Dioxepane (\(20\)) with TMSOTf-Et\(_3\)SiH

The reaction of \(12a\) is representative. To a solution of \(12a\) (380 mg, 2.2 mmol) in \(\text{CH}_2\text{Cl}_2\) (30 mL) were added \(\text{Et}_3\text{SiH}\) (1.1 g, 9.7 mmol) and then TMSOTf (1.1 g, 4.8 mmol) in 10 min and the mixture was stirred at -70 °C for 1 h under nitrogen atmosphere. After treated as above, the residue was separated by column chromatography on silica gel. Elution with ether-hexane (5:95) gave the tetrahydrofuran (\(16a\)) (157 mg, 51%).

3-Methyl-2-oxabicyclo[4.3.0]nonane (\(16a\))

A colorless oil, \(^1\text{H} \text{NMR } \delta 1.30 \text{ (d, } J = 5.94 \text{ Hz, 3 H)}, 1.20-2.13 \text{ (m, 11 H)}, 3.75-3.78 \text{ (m, 1 H)}; \(^{13}\text{C NMR } \delta 21.21, 22.84, 24.06, 28.70, 29.20, 38.13, 39.36, 74.07, 77.40; \text{HRMS (M}^+\text{) } m/z \text{ calcd for C}_9\text{H}_{16}\text{O: 140.1201, Found: 140.1202.}

4-Iodomethyl-4-methyl-2,3-dioxabicyclo[5.4.0]undecane (21)

An oil; \(^1\text{H} \text{NMR } \delta 1.21 \text{ (s, 3 H)}, 1.3-2.2 \text{ (m, 13 H)}, 3.36 \text{ (d, } J = 10.1 \text{ Hz, 1 H}), 3.48 \text{ (d, } J = 10.1 \text{ Hz, 1 H}), 4.2-4.3 \text{ (m, 1 H)}; \(^{13}\text{C NMR } \delta 16.35, 21.64, 24.03, 25.02, 26.51, 28.02, 29.63, 32.19, 38.24, 82.71, 84.58; \text{HRMS (M}^+\text{) } m/z \text{ calcd for C}_{11}\text{H}_{19}\text{IO}_2: 310.0430, \text{Found: 310.0443; Anal. Calcd for C}_{11}\text{H}_{19}\text{IO}_2: C, 42.60; H, 6.17. \text{Found: C, 43.29; H, 6.25.}

4-Iodomethyl-4-methyl-2,3-dioxabicyclo[4.4.0]decane (19)

An oil; \(^1\text{H} \delta 1.26 \text{ (s, 3 H)}, 1.1-2.0 \text{ (m, 10 H)}, 2.1-2.2 \text{ (m, 1 H)}, 3.58 \text{ (d, } J = 10.1 \text{ Hz, 1 H}), 3.64 \text{ (d, } J = 10.1 \text{ Hz, 1 H}), 3.7-3.8 \text{ (m, 1 H)}; \(^{13}\text{C NMR } \delta 12.26, 24.92, 25.39, 26.56, 28.54, 30.42, 36.77, 37.54, 79.98, 85.43; \text{HRMS (M}^+\text{) } m/z \text{ calcd for C}_{10}\text{H}_{17}\text{IO}_2: 296.0274, \text{Found: 296.0271.}

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