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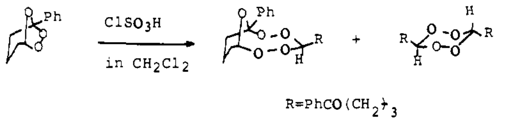
Synthesis, X-ray Analysis, and Acidolysis of *exo*- and *endo*-1-Methylindene Ozonides

Masahiro Miura,[1a] Akio Ikegami,[1a] Masatomo Nojima,*[1a] Shigekazu Kusabayashi,[1a] Kevin J. McCullough,*[1b] and Shigeru Nagase[1c]

Contribution from the Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan, the Department of Chemistry, Heriot-Watt University, Edinburgh, EH14 4AS, Scotland, and the Department of Chemistry, Faculty of Education, Yokohama National University, Hodogaya-ku, Yokohama 240, Japan. *Received August 9, 1982*

Abstract: Ozonolyses of 2,3-disubstituted 1-methylindenes gave mixtures of the corresponding exo and endo ozonides. The structures of *endo*-1-methyl-3-phenylindene ozonide (**3a**) and *exo*-1-methyl-2,3-diphenylindene ozonide (**2b**) were determined by the X-ray analysis. Acidolysis of *exo*- and *endo*-1-methylindene ozonides **2a–d** and **3a–d** under several conditions revealed some characteristic features. (a) Antimony pentachloride or chlorosulfonic acid catalyzed the interconversion of the exo–endo ozonide isomers, the ratio in equilibrium being ca. 7:3 for all the pairs. (b) In the reaction of 3-methyl-substituted indene ozonides **2c,d** and **3c,d** in acetic-d_3 acid-d a rapid hydrogen–deuterium exchange on the bridgehead methyl was observed. (c) In methylene chloride or acetic acid the ozonides decomposed very slowly, yielding the mixtures of rearranged products **4** and **5**, carboxylic acid **6**, and diketone **7**; both the rate of decomposition and the product distribution being a marked function of the structure of the ozonides. (d) Methanol accelerated the decomposition of ozonides, the disappearance following pseudo-first-order kinetics. The rate decreased in the order **3a** > **2a** > **2b** > **2c** $\simeq$ **3c** > **3b**. This order was significantly different from the order observed in the reaction in acetic acid: **3b** > **3c** > **2b** > **2c** > **3a** > **2a**. (e) Reduction by $AlHCl_2$ gave a mixture of 3,4-dihydro-1*H*-2-benzopyrans **19–22**, the composition being significantly varied depending on the stereochemistry of the ozonides. (f) Treatment of **2a** or **3a** with bis(α-hydroxy-4-methylbenzyl) peroxide (**31**) gave two stereoisomeric peroxides **32a** and **33a** in roughly equal amounts. In contrast, the reaction of an exo ozonide **2d** with a mixture of *p*-tolualdehyde and 30% H_2O_2 (an equivalent of **31**) afforded exclusively the corresponding exo peroxide **32d**, while the endo isomer **3d** gave predominantly the endo peroxide **33d**.

Acidolysis of ozonides (1,2,4-trioxolanes) has been found to proceed by several pathways depending on the structure of ozonides and reaction conditions.[2-5] Our recent investigations to develop a new synthetic method for cyclic peroxides from ozonides[6-10] have revealed that most of the reactions proceed by cleavage of the C–O bond of the peroxide bridge in the first step (eq 1 and 2). In some cases, however, evidence has been obtained which suggests that the first step of reactions involves heterolytic fission of either the C–O bond of the ether bridge (eq 3)[7] or the O–O bond (eq 4).[5] If consideration is given to the fact that most modern test involves rigorous examination of reaction stereochemistry, acidolysis of a stereoisomeric pair of ozonides might provide further insight into the mechanism. In the light of these results, we sought first to prepare the exo–endo ozonide pairs **2a–d** and **3a–d** by the ozonlysis of 1-methylindenes **1a–d** in CCl_4; the structures of *endo*-1-methyl-3-phenylindene ozonide (**3a**) and *exo*-1-methyl-2,3-diphenylindene ozonide (**2b**) were determined by the X-ray analysis. Then, the acidolysis of these ozonides was investigated under several conditions.



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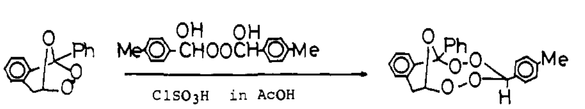
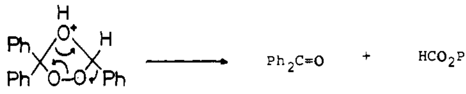


(2)

2e



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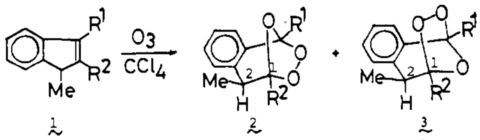
Results and Discussion

Preparation of a Pair of Exo–Endo Ozonides. When 1-methyl-3-phenylindene (**1a**) was ozonized in CCl_4 at 20 °C, a mixture of two isomeric ozonides was obtained in a yield of 72% (the **2a**/**3a** ratio = 66:34) (eq 5). The products were separated by column chromatography on silica gel. The major isomer, the C2 hydrogen of which appeared in ^{1}H NMR spectrum at a higher field (δ 3.12) with a smaller $J_{H_1-H_2}$ ($\sim$0 Hz), and the minor one [δ 3.52 (qxd, $J_{H_1-H_2}$ = 2.6 Hz, H-2)] were assigned as an exo ozonide **2a** and the endo isomer **3a**, respectively, by analogy with



(5)

1	2	3
a: R^1=Ph, R^2=H	a: R^1=Ph, R^2=H	a: R^1=Ph, R^2=H
b: R^1=R^2=Ph	b: R^1=R^2=Ph	b: R^1=R^2=Ph
c: R^1=Me, R^2=Ph	c: R^1=Me, R^2=Ph	c: R^1=Me, R^2=Ph
d: R^1=Me, R^2=H	d: R^1=Me, R^2=H	d: R^1=Me, R^2=H

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(1) (a) Osaka University. (b) Heriot-Watt University; for the X-ray analysis the correspondence should be addressed to K. J. M. (c) Yokohama National University.

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Table I. Ozonolysis of 1-Methylindenes[a]

indene	ozonides: exo/endo ratio[b]	ozonides: yield,[c] %
1a	66:34	72
1b	29:71	93
1c	25:75	83
1d	67:33	10[d]

[a] Ozonolysis was performed in CCl_4 at 20 °C. [b] The ratio of stereoisomeric ozonides was determined by ^1H NMR spectroscopy after isolation. [c] The isolated yield. [d] Polymeric products were formed in a considerable amount.

Table II. Pseudo-First-Order Rate Constants for the Reaction in Acetic Acid or Methanol

ozonide	AcOH[a]: k, s^{-1}	AcOH[a]: k_{rel}[c]	MeOH[b]: k, s^{-1}	MeOH[b]: k_{rel}[c]
2e	1.2×10^{-3}	1	9.8×10^{-3}	1
2a	9.6×10^{-5}[d]	8.0×10^{-2}	1.0×10^{-3}	1.0×10^{-1}
3a	1.4×10^{-4}	1.2×10^{-1}	2.3×10^{-3}	2.3×10^{-1}
2b	2.0×10^{-4}	1.7×10^{-1}	2.6×10^{-4}	2.7×10^{-2}
3b	2.6×10^{-4}[d]	2.2×10^{-1}	1.7×10^{-4}	1.7×10^{-2}
2c	1.5×10^{-4}	1.3×10^{-1}	2.3×10^{-4}[d]	2.3×10^{-2}
3c	2.3×10^{-4}[d]	1.9×10^{-1}	2.3×10^{-4}[d]	2.3×10^{-2}

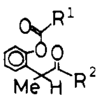
[a] The NMR spectra of a solution of an ozonide (0.2 mmol) and $ClSO_3H$ (0.02 mmol) in CD_3CO_2D-$CDCl_3$ (1 mL, 1:1 v/v) were measured periodically. [b] The NMR spectra of a solution of an ozonide (0.2 mmol) and $ClSO_3H$ (0.02 mmol) in CD_3OD-$CDCl_3$ (1 mL, 1:1 v/v) were measured periodically. [c] Relative reactivity based on **2e**. [d] The decrease in total percentage of the stereoisomeric pair of the ozonides was followed.

the spectroscopic assignments made for the *exo*- and *endo*-1-methyl-2,3-benzobicyclo[3.2.1]octan-4-ols.[11] From 1-methylindenes **1b–d** were obtained the mixtures of exo and endo ozonides **2b–d** and **3b–d** (eq 5 and Table I).

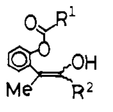
Acidolysis in Methylene Chloride or Acetic Acid. We first investigated the reaction of **2a–d** and **3a–d** in CH_2Cl_2 or AcOH to see the mode of decomposition of these ozonides in the absence of nucleophiles.

I. Kinetics and Product Analysis. The reaction of **2a–d**, **3a–d**, and 3-phenylindene ozonide (**2e**) in the presence of 0.1 equiv of $ClSO_3H$ in acetic-d_3 acid-d, was followed by periodically measuring the NMR spectrum of the reaction mixture. The disappearance of **2a–c**, **3a–c**, and **2e** followed pseudo-first-order kinetics (Table II). The data reveal the following. First, the rate of decomposition of the parent ozonide **2e** is significantly faster than those of **2a,b** and **3a,b**. It is striking that **2e** reacts 13 times faster than **2a**, this change being brought about only by the extra methyl group in **2a**. Second, the reactivities of endo ozonides **3a–c** are higher than the corresponding exo ozonides **2a–c** to a small but significant extent. Finally, the 2-phenyl-substituted indene ozonides **2b,c** and **3b,c** disappear faster than **2a** and **3a**.

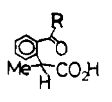
Periodic measurement of the NMR spectra of a solution of **2a** and 0.1 equiv of $ClSO_3H$ revealed the following. (a) The signals due to endo ozonide **3a** appeared immediately after the beginning of the reaction. After 30 min, equilibrium was reached and the **2a**/**3a** ratio of 7:3 remained constant during the reaction (Figure 1). (b) The NMR spectra indicated the formation of a rearranged product **5a**, a carboxylic acid **6a**, and a reduced product **7a**, the yields of which increased as the reaction proceeded. The reaction on a preparative scale afforded, along with **5a–7a**, another rearranged product **4a** (Table III), demonstrating that **4a** was formed from **5a** during workup. Similar trends for ozonide isomerization (Figure 1) and product distribution (Table III) were observed in the reaction of **3a**.



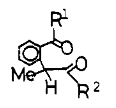
4a: R^1=Ph, R^2=H
4b: R^1=R^2=Ph
4c: R^1=Me, R^2=Ph



5a: R^1=Ph, R^2=H
5b: R^1=R^2=Ph
5c: R^1=Me, R^2=Ph



6a: R=Ph
6d: R=Me



7a: R^1=Ph, R^2=H
7b: R^1=R^2=Ph

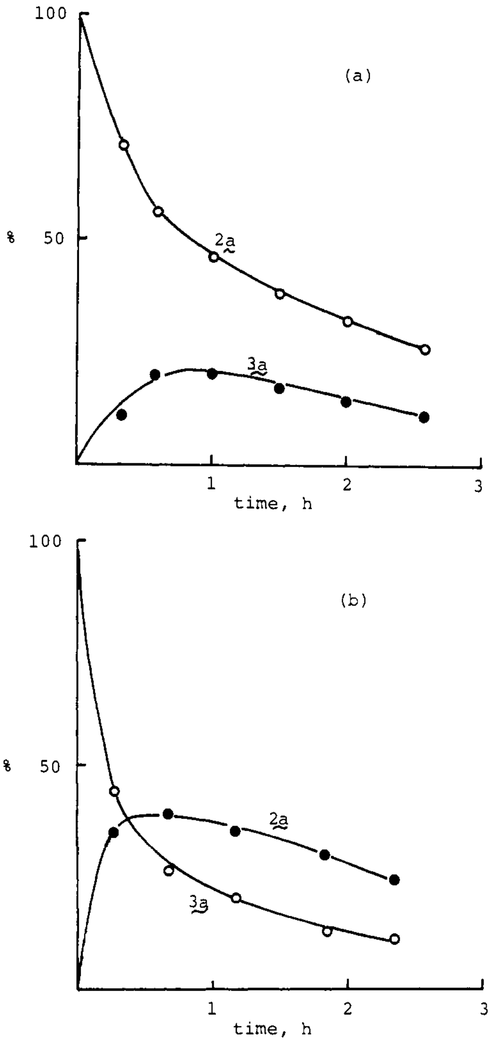
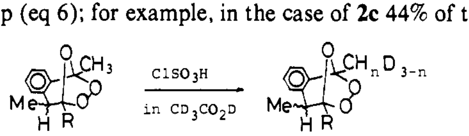


Figure 1. Reaction of **2a** (a) and **3a** (b) in the presence of $ClSO_3H$ in acetic-d_3 acid-d. Only the percentage of **2a** and that of **3a** were indicated.

The following characteristics were observed in the reaction of **2b–d** and **3b–d**. First, endo ozonides **3b–d** underwent slow isomerization to the corresponding exo isomers **2b–d** (Figure 2), and in direct contrast, the latter ozonides **2b–d** did not isomerize under the same conditions (Table IV). Second, the reaction of 3-methyl-substituted indene ozonides **2c,d** and **3c,d** in acetic-d_3 acid-d underwent rapid hydrogen–deuterium exchange on the methyl group (eq 6); for example, in the case of **2c** 44% of the hydrogen atoms were replaced by deuterium atoms after 1 h. Finally, the reaction of **2b,c** and **3b,c** gave mainly the rearranged products **4b,c** and **5b** (Table III): However, the NMR spectra of a solution of **2b** or **3b** showed the existence of only one rearranged product **5b**, whereas in the case of **2c** or **3c** the formation of **4c** and **5c** was observed.



(6)

II. Acid-Catalyzed Equilibration of Stereoisomeric Pairs of Ozonides. To understand the difference in behavior between exo–endo ozonide isomers, it is important to know their relative stabilities. With the above in mind, we determined the ozonide exo/endo ratio in equilibrium by performing reaction in the

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Table III. Reaction of Ozonides in the Presence of $ClSO_3H$: Product Distribution

ozonide	solvent	reactn time, h	products (% yield)	recovered ozonide, %
2a + 3a	$CH_2Cl_2{}^a$	3	4a (12), 5a (3), 6a (11), 7a (10)	64
2b + 3b	$CH_2Cl_2{}^a$	10	4b (29), 5b (6) 7b (36)	26
2c + 3c	$CH_2Cl_2{}^a$	8	4c (90)	
2e	$CH_2Cl_2{}^{a,c,d}$	1.5	6e (42), 13e (9)	
2a + 3a	AcOH^b	44	4a (11), 5a (9), 6a (44), 7a (18)	12
2b + 3b	AcOH^b	5	4b (10), 5b (18), 7b (10)	59
2c	AcOH^b	8	4c (76)	22^e
3c	AcOH^b	8	4c (92)	
2d	AcOH^b	24	6d (6)^f	55^e
2e	AcOH^b	2	4e (6), 6e (45), 13e (17)	

[a] A mixture of an ozonide (10 mmol) and $ClSO_3H$ (1 mmol) in CH_2Cl_2 (45 mL) was kept at 20 °C unless otherwise specified. [b] To a solution of an ozonide (3 mmol) in acetic acid (40 mL)-CH_2Cl_2 (15 mL) was added a methylene chloride solution (3 mL) of $ClSO_3H$ (0.03 mmol), and the reaction was continued at 20 °C. [d] Taken from the data in ref 8. [e] Only exo ozonide was isolated. [f] Polymeric products were also obtained.

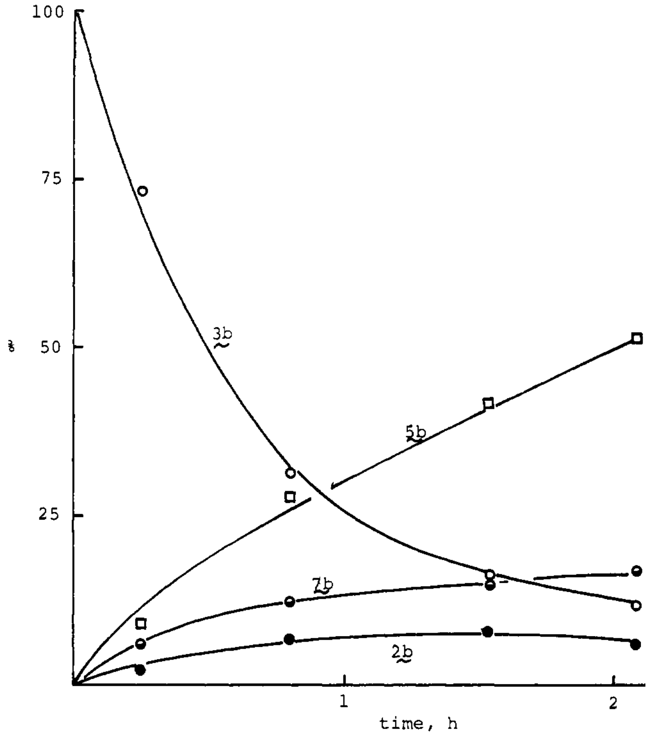
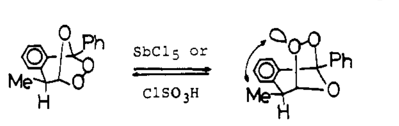


Figure 2. Reaction of **3b** in the presence of $ClSO_3H$ in acetic-d_3 acid-d.

presence of $SbCl_5$ or $ClSO_3H$ in CH_2Cl_2 (Table IV). The reaction of **2a** or **3a** with 0.1 equiv of $SbCl_5$ in CH_2Cl_2 gave an equilibrium mixture of **2a** and **3a** in a ratio of 7:3 (eq 7). For the pairs **2b–3b**



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and **2c–3c**, the exo/endo ratios in equilibrium were also ca. 7:3. These results demonstrate that exo ozonides **2a–c** are thermodynamically more stable than the endo isomers **3a–c**: This fact is consistent with (a) endo ozonides **3a–c** decomposing faster than the exo isomers **2a–c** (Table II), and (b) in acetic acid, endo ozonides **3b,c** isomerize to **2b,c**, while in the case of the exo ozonides **2b,c** this isomerization was not observed (Table IV). Molecular models suggest the greater steric interaction between the methyl group and the adjacent peroxidic oxygen in **3a–c** contributes to the relatively decreased stabilities of these ozonides.

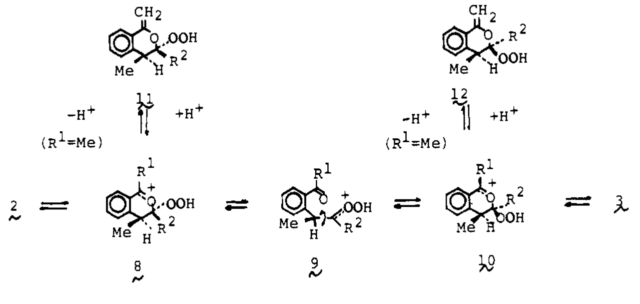
Chlorosulfonic acid in methylene chloride was also an effective catalyst to bring about the interconversion of **2** and **3** (Table IV). The product distributions in these reactions were much the same as those observed in the reactions in acetic acid (Table III). This fact indicates that acetic acid with a low nucleophilicity does not play an important role in determining product composition. It should be noticed, however, the rate of ozonide isomerization in CH_2Cl_2 was remarkably different from that in acetic acid (Table IV).

Table IV. Isomerization of Exo and Endo Ozonides[a]

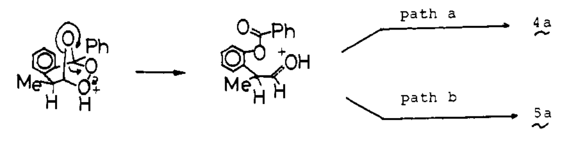
ozonide	catalyst	solvent	reactn time, h	recovered ozonides %	exo/endo ratio
2a	$SbCl_5$	CH_2Cl_2	2	21	71:29
3a	$SbCl_5$	CH_2Cl_2	2	28	69:31
2b	$SbCl_5$	CH_2Cl_2	1	44	67:33
3b	$SbCl_5$	CH_2Cl_2	1	44	67:33
2c	$SbCl_5$	CH_2Cl_2	1	65	73:27
3c	$SbCl_5$	CH_2Cl_2	1	67	67:33
2d	$SbCl_5$	CH_2Cl_2	1	35	87:13
3d	$SbCl_5$	CH_2Cl_2	1.5	60	30:70
2a	$ClSO_3H$	CH_2Cl_2	4	62	72:28
3a	$ClSO_3H$	CH_2Cl_2	5	43	69:31
2b	$ClSO_3H$	CH_2Cl_2	2	70	74:26
3b	$ClSO_3H$	CH_2Cl_2	2	69	69:31
2c	$ClSO_3H$	CH_2Cl_2	2	68	79:21
3c	$ClSO_3H$	CH_2Cl_2	2	75	33:67
2a	$ClSO_3H$	AcOH	24	21	67:33
3a	$ClSO_3H$	AcOH	24	8	68:32
2b	$ClSO_3H$	AcOH	4	42	100:0
3b	$ClSO_3H$	AcOH	4	48	32:68
2c	$ClSO_3H$	AcOH	8	53	100:0
3c	$ClSO_3H$	AcOH	4	58	35:65
2d	$ClSO_3H$	AcOH	8	62	100:0
3d	$ClSO_3H$	AcOH	4	51	13:87

[a] The reaction was performed in the presence of 0.1 molar equiv of an acid catalyst.

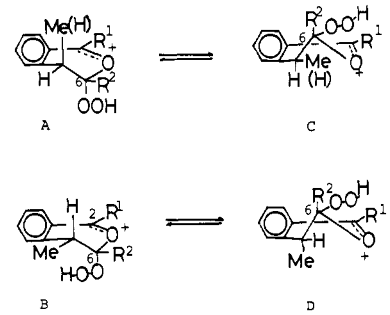
Scheme I



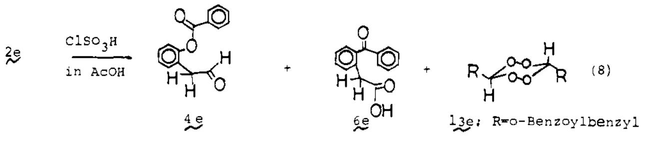
Scheme II



III. Mechanistic Aspects. What is the mechanistic origin of the interconversion of exo–endo ozonide isomers? For the interconversion to occur, the cleavage and reformation of two of the C–O bonds of an ozonide would be required.[12] When the ease in cleavage of the C–O bond of the peroxide bridge by an acid catalyst is considered,[6-10] the first step of the reaction of **2** must involve the formation of a carboxonium ion **8** followed by electron migration to afford a protonated carbonyl oxide **9**, as shown in Scheme I. Subsequent C–C bond rotation, followed by rebonding of the carbonyl oxygen and the positive carbon, would yield two carboxonium ions **8** and **10**, which in turn would give **2** and **3**, respectively. Fast hydrogen–deuterium exchange observed in the acidolysis of ozonides **2c,d** and **3c,d**, having a bridgehead methyl, in acetic-d_3 acid-*d* (eq 6) may be best rationalized in terms of a process involving rapid deprotonation–protonation between carboxonium ion **8** or **10** and vinyl ether **11** or **12** (Scheme I). Thus, this fact also suggests that, even in acetic acid, formation of carboxonium ions **8** and **10** is a facile process. However, the reverse reaction is extremely fast, and as a result the disappearance of ozonides occurs very slowly. Examination of the structure of carboxonium ions **8a–d** and **10a–d** by models provides an appropriate solution to the remarkable behavior of **2a–d** and **3a–d**. The conformations of the carboxonium ions **8** and **10** first formed from **2** and **3** are represented as A and B, respectively, in which the nucleophilic hydroperoxy substituent occupies the pseudoaxial position. Ring deformation may lead to conformations C (from A) and D (from B), with the hydroperoxy group occupying the pseudoequatorial position. It seems likely that carboxonium ions **8** and **10** would preferentially adopt conformations A and B rather than C and D for the following reasons: (a) The unfavorable gauche methyl–hydroperoxy interaction in conformation C would be expected to destabilize it with respect to A, and (b) the deformation from B to D is subject to a severe methyl–hydroperoxy interaction. In addition, carboxonium ions **8** and **10**, having a bulky phenyl group at position-6 prefer to place the substituent equatorially, with these carboxonium ions existing as conformations A and B almost exclusively. Thus, in the absence of appropriate nucleophiles, regeneration of ozonides **2** and **3** should be a most favorable process in decay of **8** and **10**. In the case of **2e**, lacking an extra methyl group, the interconversion of two conformers A and C would be, however, a more facile process.



Formation of rearranged products **4** and **5**, carboxylic acid **6**, and reduced product **7** from **2a–d** and **3a–d** is in marked contrast to the fact that under similar conditions 1-phenylcyclopentene ozonide gives two dimerization products in good yields (eq 1). The latter is a major route in decomposition of less highly substituted (compared with **2a**) bicyclic and monocyclic ozonides.[6,7] In harmony with this, the reaction of 3-phenylindene ozonide (**2e**) with 0.1 equiv of $SbCl_5$ in CH_2Cl_2 gave a dimerization product **13e** in 30% yield.[7] Treatment of **2e** with $ClSO_3H$ in acetic acid afforded **13e** in 17% yield, along with **4e** and **6e** (eq 8 and Table III). This change in product composition may be brought about by the steric bulk of the ozonides **2a–c** and **3a–c** which forces ozonide dimerization via the carboxonium ions **8** and **10** to be difficult.[7]



Scheme III

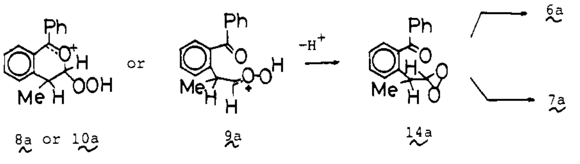


Table V. Reaction in Methanol[a]

ozonide	reactn time, h	product (% yield)	recovered ozonide %	recovered ozonide exo/endo ratio
2a	4	15a (37), 17a (28)	21	100/0
3a	2	16a (36), 17a (33)	8	0/100
2b	8	7b (55)	40	100/0
3b	8	7b (45)	48	36/64
2c	6	4c (36)	53	68/32
3c	6	4c (26)	58	62/38
2d	24	15d (7)	62	100/0
2e[b,c]	4	15e (37), 16e (39)		

[a] The reaction of an ozonide (1 mmol) and $ClSO_3H$ (0.1 mmol) in methanol–methylene chloride (20 mL, 1:1 v/v) was performed at 20 °C unless otherwise stated. [b] The reaction in the presence of 0.03 equiv of $ClSO_3H$. [c] Taken from the data in ref 18.

A brief comment may be necessary on the formation of **4–7**. A mechanism shown in Scheme II rationalizes the formation of rearranged products **4** and **5** most reasonably.[5] This mechanism involves heterolytic O–O bond fission in the first step, followed by concerted migration of the fused benzene ring. In the final step, loss of proton attached to either the oxygen (path a) or the carbon (path b) takes place to yield **4** and **5**, respectively. As the NMR data suggest, the latter path seems to be extremely favored in the case of **2a,b** and **3a,b**. Carboxonium ions **8** and **10** (or protonated carbonyl oxide **9**) may mainly concern the formation of **6** and **7** (Scheme III): Carboxylic acid **6** may be formed from **8** and **10** (or **9**) via **14**,[13] and reduction by adventitious water or acetic acid may give **7**.[14,15] However, other possibilities remain to be considered[16,17] and therefore further investigations must be

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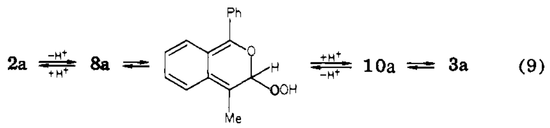
[12] Alternatively, a mechanism involving deprotonation–protonation between carboxonium ions, **8a** or **10a**, and **39** may be considered (eq 9). However, the fact that the ozonides **2a** and **3a** recovered from the reaction of **2a** or **3a** in the presence of $ClSO_3H$ in acetic-d_3 acid-*d* did not contain deuterium seems to exclude this possibility. If the interconversion proceeds by this mechanism, the hydrogen attached to the carbon bearing a methyl group should have been replaced by deuterium in a considerable amount.



39

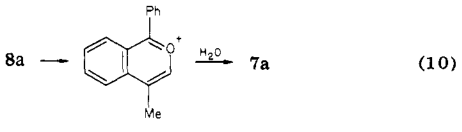
[13] The importance of this process in a gas-phase ozonolysis has been proposed by Harding and Goddard: Harding, L. B.; Goddard, W. A., III. *J. Am. Chem. Soc.* **1978**, *100*, 7180.

[14] The interconversion of a (protonated) carbonyl oxide as one of the precursors of **7** has been proposed by several groups.[15]

[15] (a) Bartlett, P. D.; Baumstark, A. L.; Landis, M. E. *J. Am. Chem. Soc.* **1977**, *99*, 1890. (b) Miura, M.; Nojima, M.; Kusabayashi, S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1950.

[16] For the formation of carboxylic acid **6**, a process involving cleavage of the C–O bond of the ether bridge (eq 3) may also participate to some extent.[7]

[17] As an alternative process leading to reduction product 7, a mechanism illustrated in eq 10 may be considered. In fact, in the reaction in $CHCl_3$ a precipitate attributable to a pyrylium salt **40** was separated in a detectable amount.[8]



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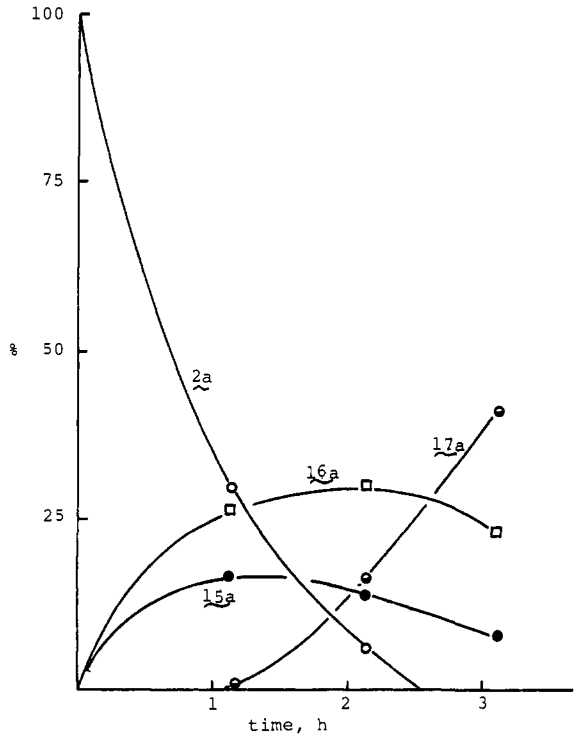


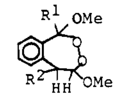
Figure 3. Reaction of **2a** in the presence of $ClSO_3H$ in methanol-d_4.

undertaken to understand the precise nature of the transformation involved.

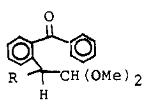
In summary, acid catalysts can easily break the C–O bond of the peroxide bridge of ozonides **2a–d** and **3a–d** affording carboxonium ions **8a–d** and **10a–d**. However, the paths leading to products **6** and **7** and a reverse reaction to regenerate ozonides participate competitively, the latter being extremely favored. Therefore, a process involving O–O bond cleavage (Scheme III) becomes an important route in the rearrangement of the ozonides. This conclusion leads to an expectation that in the presence of an appropriate nucleophile with an ability to capture intermediate carboxonium ions **8** and **10**, the products via these intermediates would be obtained predominantly. On this basis, we investigated next the acidolysis of the ozonides in the presence of nucleophiles.

Acidolysis in Methanol. The reaction of ozonides **2a–c** and **3a–c** in the presence of 0.1 equiv of $ClSO_3H$ in methanol-d_4 was followed by measuring the NMR spectra periodically. The disappearance of the ozonides follows pseudo-first-order kinetics (Table II). The rate decreases in the order **2e** > **3a** > **2a** > **2b** > **2c** ≃ **3c** > **3b**. The order **2a** > **2b** and the order **2b** > **3b** were found to be the reverse of those observed in the reaction in acetic acid. Moreover, the rates of reaction of **2a**, **3a**, and **2e** in methanol are significantly faster than those in acetic acid, contrary to the expectation that acid strength is considerably lower in a more basic solvent such as methanol than in acetic acid. Cleavage of the C–O bond of the peroxide bridge, therefore, normally takes place more easily in the latter solvent.

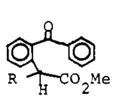
Periodic measurement of the NMR spectra of a solution of **2a** and 0.1 equiv of $ClSO_3H$ revealed the following. (a) Isomerization to **2a** was not observed during the reaction. (b) The reaction afforded a mixture of hemiperacetal **15a**, acetal **16a**, and ester **17a**, the yields of which increased as the reaction proceeded (Figure 3). The reaction on a preparative scale afforded **15a** and **17a** (Table V). Ozonide isomerization was also not observed for **3a,d** and **2b,d**. In contrast, **3b** isomerized slowly to **2b** under the same conditions. Diketone **7b** was the sole product from **2b** and **3b**, which is in marked contrast to the predominant formation of rearranged products **4b** and **5b** in acetic acid. The hemiperacetal **15d** was obtained from **2d** and **3d**. In methanol-d_4 this reaction was accompanied by rapid hydrogen–deuterium exchange on the bridgehead methyl group (see eq 6). After 5 h, 65% of the methyl hydrogens of **2d** had been replaced by deuteriums.



15a: R1=Ph, R2=Me
15d: R1=R2=Me
15e: R1=Ph, R2=H



16a: R=Me
16e: R=H



17a: R=Me
17e: R=H

Scheme IV

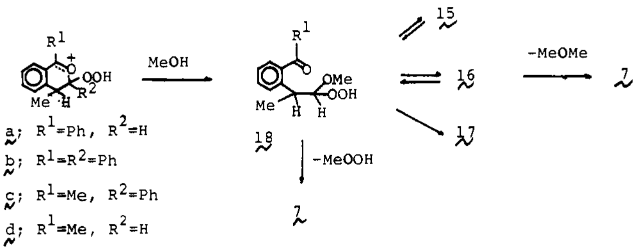
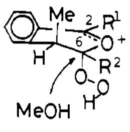


Table VI. Reaction with Dichloroaluminum Hydride

ozonide	reductant (proportion)	reactn time, h	3,4-dihydro-1H-2-benzopyran^a yield, %	composition 19	20	21	22
2a	$AlDCl_2$ (4)	1	17	58	32	4	6
3a	$AlDCl_2$ (8)	2	22	44	18	16	22
2a	$AlHCl_2$ (8)	1	42	95^b		5^c	
3a	$AlHCl_2$ (8)	1	18	40^b		60^c	
2b	$AlHCl_2$ (4)	2	45	66	29	9	
3b	$AlHCl_2$ (4)	2	44	20		80	
2c	$AlHCl_2$ (8)	1	24	80	20		
3c	$AlHCl_2$ (8)	1	36	40		60	
2d	$AlDCl_2$ (8)	1	44	80^d		9	10
3d	$AlHCl_2$ (8)	1	17	41^b		59^c	

[a] As a byproduct the diol 24a–d was obtained in a considerable amount. [b] The composition of *cis*-1-phenyl-4-methyl- or *cis*-1,4-dimethyl-3,4-dihydro-1*H*-2-benzopyran. [c] The composition of *trans*-1-phenyl-4-methyl- or *trans*-1,4-dimethyl-3,4-dihydro-1*H*-2-benzopyran. [d] The sum of 19d and 20d.

A reasonable precursor of the products **15–17** is the corresponding α-methoxy hydroperoxide **18**.[18] In methanol **7b** may be formed from **16b** or **18b** (Scheme IV). Solvation of carboxonium ions **8** and **10** by methanol, irrespective of the extent, would provide a substantial energy lowering of the process leading to **18** which in turn would favor this pathway in this solvent. Examination of the structure of carboxonium ions **8** and **10** by models gives an appropriate solution to the following questions. (a) The more stable exo ozonide **2b** reacts faster than **3b**, and (b) the rates of reaction of **2a** and **3a** in methanol are significantly faster than those in acetic acid (Table II). Methanol would be expected to attack the 6-position of **8** or **10** from the rear side of the ether linkage. Approach of methanol to **10b** at this position would be, however, considerably hindered by the phenyl ring and the methyl group, both of which occupy the pseudoequatorial positions. In the case of **8b**, in which the two substituents are cis related, the hindrance would be relatively small. Since the capture of less hindered **8a** and **10a** by methanol is likely to be extremely fast, ozonide isomerization would be completely depressed. It should be noticed that in acetic acid isomerization of **3a** to **2a** is sig-



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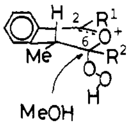

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(18) Miura, M.; Nojima, M.; Kusabayashi, S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2909.

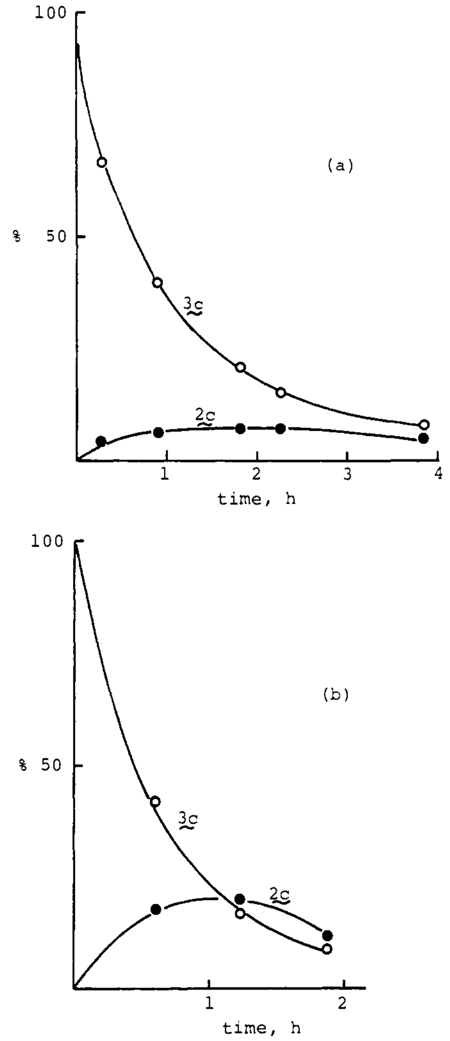


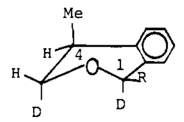
Figure 4. Reaction of **3c** in the presence of $\mathrm{ClSO_3H}$ in acetic-d_3 acid-d (a) or in methanol-d_4 (b). Only the percentage of **3c** and that of **2c** were indicated.

nificantly faster than that of **3b** to **2b** (Figures 1 and 2).

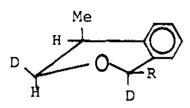
The behavior of **2c** and **3c** in methanol is striking. (a) The interconversion of **2c** to **3c** proceeds rapidly, the rate being considerably faster than that in acetic acid (Figure 4). (b) A rearranged product **4d** is the sole observed product (Table V and Scheme II). The reason for the unexpected behavior of **2c** and **3c** is obscure.

Reaction with Dichloroaluminum Hydride. Powerful nucleophiles would possibly attack carboxonium ions **8** and **10** at the 2-position, giving rise to the mixtures of stereoisomeric 3,4-dihydro-1*H*-2-benzopyrans.[19] Thus, the variable product composition as a function of the stereochemistry of the ozonides **2** and **3** might provide valuable information regarding the acidolysis mechanism of the ozonides. With the above in mind, we investigated the reaction of **2a–d** and **3a–d** with $\mathrm{AlHCl_2}$ and found that the reaction proceeds stereospecifically (Table VI).

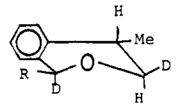
Treatment of **2a** with 8 molar equiv of $\mathrm{AlDCl_2}$ (prepared by mixing $\mathrm{LiAlD_4}$ and 3 molar equiv of $\mathrm{AlCl_3}$[20]) in ether gave, along with 1-phenyl-4-methyl-1*H*-2-benzopyran-1-*d* (**23**) and the dideuterated diol **24a**, the four dideuterated 3,4-dihydro-1*H*-2-benzopyrans **19a–22a**. This result demonstrates that the two C–O bonds of the peroxide bridge of **2a** had been replaced by deuterium atoms. By ^{1}H NMR spectroscopy, the ratio of the products **19a–22a** was found to be 58:32:4:6. From **2d** was obtained a mixture of the dideuterated 2-benzopyrans **19d–22d**, the composition being similar to that observed in the reaction of **2a** (however, in this case the **19d**/**20d** ratio could not be determined).



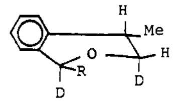
19a: R=Ph
19d: R=Me



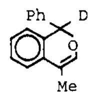
20a: R=Ph
20d: R=Me



21a: R=Ph
21d: R=Me



22a: R=Ph
22d: R=Me



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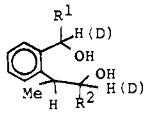
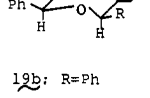


24a: $\mathrm{R^1{=}Ph,\ R^2{=}H}$
24b: $\mathrm{R^1{=}R^2{=}Ph}$
24c: $\mathrm{R^1{=}Me,\ R^2{=}Ph}$
24d: $\mathrm{R^1{=}Me,\ R^2{=}H}$

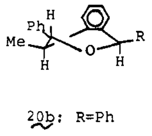
Dichloroaluminum hydride is well-known to reduce acetals to the corresponding ethers.[20] A proposed mechanism involves heterolytic cleavage of the ether linkage to provide a carbocationic intermediate, followed by hydride transfer from $\mathrm{AlHCl_2}$ or $\mathrm{AlH(OR)Cl_2^-}$. As a reasonable extrapolation, the reaction of **2a** with $\mathrm{AlDCl_2}$ is postulated to proceed by C–O bond fission of the peroxide bridge in the first step to yield the carboxonium ion **25a** (Scheme V). Intramolecular attack by deuteride ion from the side opposite to the methyl group (path a) would afford **27a** and intermolecular attack by excess $\mathrm{AlDCl_2}$ from the reverse side (path b) would yield **28a**.[20] Subsequent departure of $^-\mathrm{OOAlCl_2}$ would produce the carboxonium ions **29a** (from **27a**) and **30a** (from **28a**), respectively. Dueteride transfer to **29a** would give either **19a** (path c) or **20a** (path d), depending on the direction of the attack. A similar reaction sequence via **30a** would afford either **21a** (path e) or **22a** (path f). The exclusive formation of **19a–22a** suggests that the second deuteride transfer is substantially faster than the first one.

Product distributions, coupled with a proposed mechanism shown in Scheme V, reveal the following: (a) The extremely high (**19a** + **20a**)/(**21a** + **22a**) ratio of 9:1 indicates deuteride transfer to **25a** occurs preferentially from the less hindered side (path a); attack from the opposite side (path b) is prevented by the pseudoaxial methyl group to a considerable extent. (b) The **19a**/**20a** ratio 7:3 suggests that attack on **29a** takes place mainly from the direction opposite to the methyl group (path c). (c) However, the **21a**/**22a** ratio 2:3 suggests that the attack of deuteride ion on **29a** is not highly stereoselective (path e and f). If the carboxonium ion **30a** were roughly planar, this result is understandable; path e would be disfavored due to the hindrance by the phenyl group whereas the methyl group would retard the approach of the nucleophile syn to the substituent (path f).

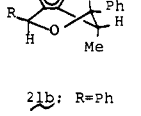
The reaction of **2b,c** with $\mathrm{AlHCl_2}$ revealed the following. An exo ozonide **2b** gave the three 2-benzopyrans **19b–21b** in a ratio 7:2:1, while from **2c** was obtained a mixture of only the two



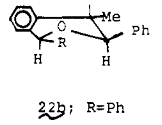
19b: R=Ph
19c: R=Me



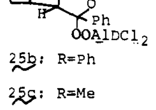
20b: R=Ph
20c: R=Me



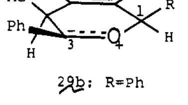
21b: R=Ph
21c: R=Me



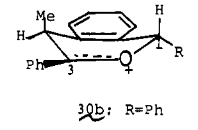
22b: R=Ph
22c: R=Me



25b: R=Ph
25c: R=Me



29b: R=Ph
29c: R=Me



30b: R=Ph
30c: R=Me

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[19] Perst, H. "Carbonium Ions"; Wiley: New York, 1976; pp 1961–2047.

[20] (a) Eliel, E. L. *Rec. Chem. Prog.* **1961**, *22*, 129. (b) Eliel, E. L.; Nader, F. W. *J. Am. Chem. Soc.* **1970**, *92*, 3045. (c) Ashby, E. C.; Prather, J. *Ibid.* **1966**, *88*, 729. (d) Lansburg, P. T.; Scharf, D. J.; Pattison, V. A. *J. Org. Chem.* **1967**, *32*, 1748.

Scheme V

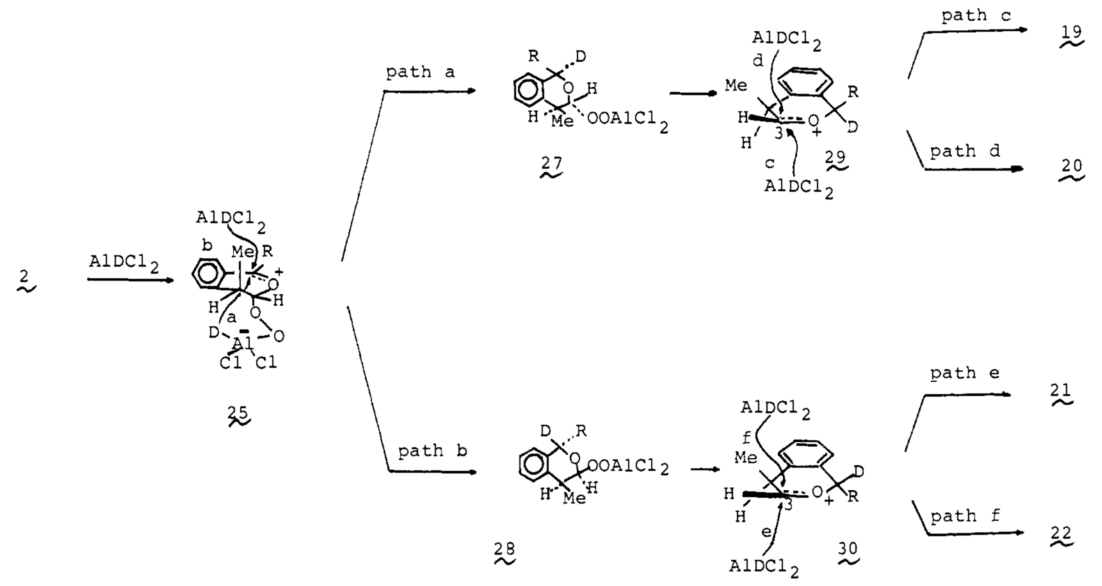


Table VII. Reaction with Bis(α-hydroxy-4-methylbenzyl) Peroxide (31)[a] or with a Mixture of *p*-Tolualdehyde and 30% Hydrogen Peroxide[b]

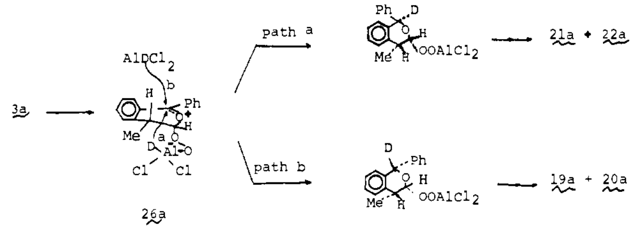
ozonide	reagent	reactn time, h	cyclic peroxide yield, %	cyclic peroxide exo/endo	recovered ozonide %	recovered ozonide exo/endo
2a	*p*-tolualdehyde-30% H_2O_2	2	13	50:50	13[c]	
2a	31	4	9	46:54	25	70:30
3a	31	8	10	46:54	33	68:32
2d	*p*-tolualdehyde-30% H_2O_2	4	7	100:0	51	100:0
3d	*p*-tolualdehyde-30% H_2O_2	4	6	9:91	51	13:87
2e	31	0.3	31[d]			
2e	*p*-tolualdehyde-30% H_2O_2	4	27[d]			

[a] The reaction of an ozonide (2 mmol) with 31 (2 mmol) in the presence of $ClSO_3H$ (0.2 mmol) in acetic acid (15 mL) was performed at 20 °C. [b] The reaction of an ozonide (3 mmol) with a mixture of *p*-tolualdehyde (6 mmol) and 30% H_2O_2 (6 mmol) in the presence of $ClSO_3H$ (0.3 mmol) in acetic acid (25 mL). [c] The exo/endo ratio was not determined. [d] Taken from the data in ref 9.

2-benzopyrans **19c** and **20c** in a ratio of 4:1 (Table V). A large (**19b** + **20b**)/**21b** ratio and the absence of **21c** and **22c** in the products from **2c** are consistent with a high (**19a** + **20a**)/(**21a** + **22a**) ratio from **2a**, suggesting that path a dominates in all the carboxonium ions **25a–d**. The high **19b**/**20b** ratio 7:2 and the absence of **22b** in the products demonstrate that hydride transfer to both **29b** and **30b** also proceeds with high stereospecificity. If the structure of **29b** and **30b** is taken into consideration, this result is understandable. In the case of **29b** both the methyl group and the phenyl ring at the 1-position would accelerate the attack by hydride ion at the 3-position from the less hindered side, whereas in the case of **30b** the pseudoaxial methyl group would force the nucleophile to approach from the less hindered side. It is noticed that in the most preferable conformation the pyran ring of **30b** is slightly distorted to minimize the substituent–substituent interaction. In contrast, the carboxonium ion **30a** from **2a** is considered to have a planar geometry (Scheme V). In summary, in the reaction of exo ozonides **2a–d** hydride transfer to a carboxonium ion **25a–d** occurs predominantly from the less hindered side (path a). Hydride transfer to **29a–d** is also stereoselective, with the **19**/**20** ratio increasing with the increase in steric bulk of the substituent at the 3-position.

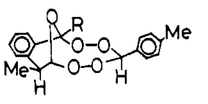
The endo ozonides **3a–d** also gave the mixtures of **19–22**, in which the compositions were remarkably different from those observed in the reaction of **2a–d**. From **3a** were obtained **21a** and **22a** in considerable amounts, along with **19a** and **20a**. The (**19a** + **20a**)/(**21a** + **22a**) ratio 3:2 suggests that the hydride ion attacks the carboxonium ion **26a** almost equally from both directions (paths a and b in Scheme VI). The same trend was also observed in the reaction of **3c,d**. Molecular models suggest that in **26a** the methyl group occupies the pseudoequatorial position, with attack by the hydride ion not being significantly inhibited by this substituent. Absence of **20b,c** and **22b,c** in the products from **3b,c** is interpreted as exclusive transfer of hydride ion to **29b,c** and **30b,c** from the less hindered side, this trend being much the same as that observed in the reaction of **2b,c**.[21]

Scheme VI

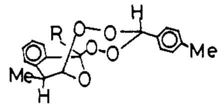


Reaction with Bis[α-hydroxy-4-methylbenzyl] Peroxide (31). We recently reported that the reaction of **2e** with **31** or a mixture of tolualdehyde and 30% H_2O_2 (an equivalent of **31**),[22] gives a bicyclic peroxide having a unique structure (eq 2 and Table VII).[9] To obtain further insight into the mechanism, the reactions of **2a–d** and **3a–d** with these reagents were investigated.

The reaction of **2a** with 1 molar equiv of **31** in the presence of 0.1 equiv of $ClSO_3H$ in acetic acid gave a mixture of **32a** and



32a; R=Ph
32d; R=Me



33a; R=Ph
33d; R=Me

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[21] A mechanism shown in Scheme V, coupled with the fact that **2b** gave both **19b** and **20b** in a ratio of 7:2, suggests that **20b** also may be formed from **3b** in a small amount. However, we failed to detect it.

[22] Swern, D. "Organic Peroxide"; Interscience: New York, 1970; Vol. 1.

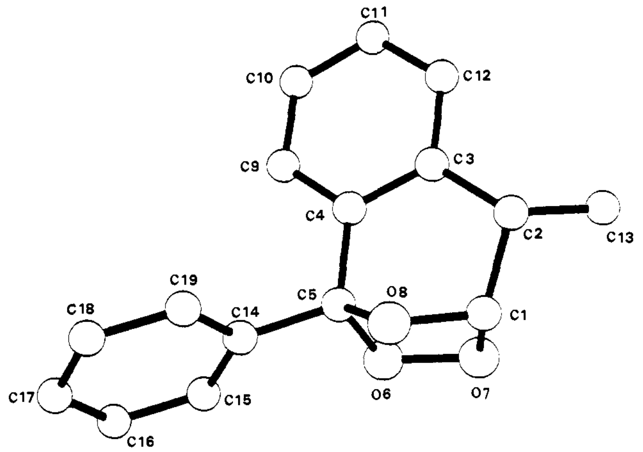

Figure 5. Crystal structure of ozonide (**3a**) as determined by X-ray analysis. The hydrogen atoms have been omitted for clarity.

Table VIII. Crystal Data for Ozonides 3a and 2b

	3a	2b
mol formula	$C_{16}H_{14}O_3$	$C_{22}H_{18}O_3$
M_r	254.29	330.38
mp, °C	151-152 (ex MeOH)	125 (ex MeOH)
a, Å	9.073 (1)	33.316 (4)
b, Å	16.281 (1)	33.316 (4)
c, Å	17.495 (2)	8.256 (1)
α, β, deg	90	90.0
γ, deg	90	120.0
V_c, Å^3	2584.2 (6)	7936 (1)
space group	orthorhombic *Pbca* (no. 61)	rhombohedral (hexagonal axes) $R\bar{3}$ (no. 148)
Z	8	18
d_{calcd}, g cm^{-3}	1.31	1.24
d_{obsd}, g cm^{-3}	1.32 (CCl_4/MeOH)	1.25 (CCl_4/MeOH)
μ, cm^{-1}	6.45	5.78

33a (the ratio ca. 1:1) in 9% yield. The recovered ozonide (25%) was found to be a mixture of **2a** and **3a**, the ratio being 7:3. Exactly the same result was obtained in the reaction of **3a** (Table VII). These facts demonstrate that acid-catalyzed equilibration of **2a** and **3a** is significantly faster than capture of the carboxonium ions **8a** and **10a** by **31**. In contrast, treatment of **2d** with a mixture of *p*-tolualdehyde and 30% H_2O_2 in the presence of $ClSO_3H$ gave **32d** exclusively, whereas, from **3d**, a mixture of **32d** and **33d** was obtained in a ratio of 9:91. These results again demonstrate that the interconversion of **2d** and **3d** is very slow in the $ClSO_3H$–AcOH system. The ozonides **2b,c** and **3b,c** did not give the corresponding cyclic peroxides. The ozonide **2e**, which would most likely produce a carboxonium ion with relatively greater flexibility, gave the corresponding bicyclic peroxide in a greater yield than the ozonides **2a,d** and **3a,d**. Molecular models suggest that only the carboxonium ions **8** and **10**, which adopt the conformations C and D, would be subject to attack at the 2-position by **31** and thereby subsequently afford the bicyclic peroxides (Scheme VII). On the other hand, the approach of the bulky peroxide **31** would be significantly hindered by the pseudoaxial hydroperoxy group in the alternative conformations A and B. Thus, if the carboxonium ions **8b,c** and **10b,c**, derived from the corresponding more highly substituted ozonides, preferentially adopt conformations A and B, then the absence of bicyclic peroxide products from the ozonides **2b,c** and **3b,c** may be more readily explained.

Scheme VII

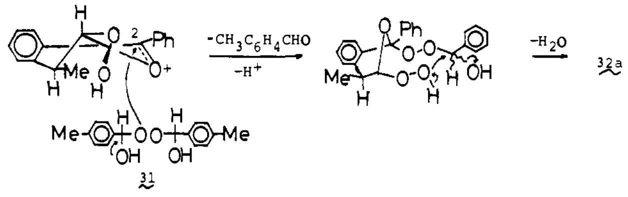

Table IX. Atomic Fractional Coordinates for $C_{16}H_{14}O_3$ (3a)

atom	x/a	y/b	z/c
C1	0.8887 (4)	0.1302 (2)	0.7380 (2)
C2	0.8674 (4)	0.0424 (2)	0.7634 (2)
C3	0.7813 (3)	−0.0040 (2)	0.7025 (2)
C4	0.7496 (3)	0.0342 (2)	0.6332 (2)
C5	0.8001 (3)	0.1217 (2)	0.6213 (1)
O6	0.7011 (2)	0.1773 (1)	0.6595 (1)
O7	0.7505 (3)	0.1744 (1)	0.7395 (1)
O8	0.9349 (2)	0.1354 (1)	0.6614 (1)
C9	0.7344 (4)	−0.0845 (2)	0.7129 (2)
C10	0.6558 (5)	−0.1255 (2)	0.6571 (2)
C11	0.6249 (5)	−0.0874 (2)	0.5895 (2)
C12	0.6714 (4)	−0.0078 (2)	0.5774 (2)
C13	0.7972 (6)	0.0392 (3)	0.8430 (2)
C14	0.8183 (4)	0.1492 (2)	0.5400 (2)
C15	0.7226 (4)	0.2031 (2)	0.5057 (2)
C16	0.7438 (6)	0.2264 (2)	0.4299 (2)
C17	0.8596 (6)	0.1960 (2)	0.3898 (2)
C18	0.9558 (5)	0.1417 (3)	0.4232 (2)
C19	0.9346 (4)	0.1184 (2)	0.4982 (2)

Table X. Atomic Fractional Coordinates for $C_{22}H_{18}O_3$ (2b)

atom	x/a	y/b	z/c
C1	0.7608 (2)	0.5968 (2)	0.6198 (6)
C5	0.7786 (3)	0.5424 (2)	0.6709 (8)
O6	0.8183 (2)	0.5768 (2)	0.5807 (6)
O7	0.8105 (2)	0.6161 (2)	0.5809 (6)
O8	0.7424 (2)	0.5485 (2)	0.6029 (6)
C2	0.7606 (5)	0.6183 (6)	0.7826 (11)
C13	0.7106 (5)	0.6070 (7)	0.8279 (22)
C3	0.7780 (6)	0.5956 (5)	0.9020 (15)
C4	0.7857 (6)	0.5603 (5)	0.8453 (10)
C9	0.7857 (6)	0.6116 (6)	1.0625 (15)
C10	0.8033 (6)	0.5920 (6)	1.1710 (18)
C11	0.8098 (6)	0.5554 (6)	1.1235 (15)
C12	0.8018 (5)	0.5411 (5)	0.9616 (14)
C20	0.7403 (2)	0.6132 (2)	0.4900 (6)
C21	0.6985 (2)	0.5825 (2)	0.4147 (6)
C22	0.6790 (2)	0.5990 (2)	0.3017 (6)
C23	0.7013 (2)	0.6461 (2)	0.2639 (6)
C24	0.7430 (2)	0.6768 (2)	0.3393 (6)
C25	0.7625 (2)	0.6604 (2)	0.4523 (6)
C14	0.7745 (6)	0.4974 (3)	0.6075 (21)
C15	0.7310 (6)	0.4573 (3)	0.6091 (21)
C16	0.7260 (6)	0.4157 (3)	0.5518 (21)
C17	0.7645 (6)	0.4141 (3)	0.4929 (21)
C18	0.8079 (6)	0.4542 (3)	0.4913 (21)
C19	0.8129 (6)	0.4959 (3)	0.5486 (21)
C2′	0.7557 (5)	0.6047 (6)	0.7985 (8)
C13′	0.7041 (5)	0.5890 (6)	0.8383 (22)
C3′	0.7741 (6)	0.5799 (5)	0.9029 (14)
C4′	0.7828 (6)	0.5448 (6)	0.8536 (9)
C9′	0.7803 (6)	0.5895 (6)	1.0688 (14)
C10′	0.7955 (6)	0.5664 (5)	1.1708 (19)
C11′	0.8018 (6)	0.5311 (6)	1.1062 (16)
C12′	0.7978 (5)	0.5192 (5)	0.9422 (14)
C14′	0.7690 (6)	0.4939 (3)	0.6333 (21)
C15′	0.7293 (6)	0.4558 (3)	0.6956 (21)
C16′	0.7198 (6)	0.4110 (3)	0.6591 (21)
C17′	0.7499 (6)	0.4043 (3)	0.5602 (21)
C18′	0.7895 (6)	0.4424 (3)	0.4978 (21)

Description of the Structures of the Ozonides and Discussion. A summary of pertinent crystal data for both ozonides **3a** and **2b** is given in Table VIII. Figure 5[23] illustrates the molecular structure obtained for *endo*-1-methyl-3-phenylindene ozonide (**3a**) along with the numbering system adopted for this study. This structure corresponds to the endo isomer with the methyl group (C13) at C2 adjacent to the peroxidic bridge, thereby verifying the previous tentative assignment. The general structural features of *exo*-1-methyl-2,3-diphenylindene ozonide (**2b**) are shown in

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[23] Motherwell, S. "PLUTO, a Program for Plotting Molecular and Crystal Structures", Cambridge.

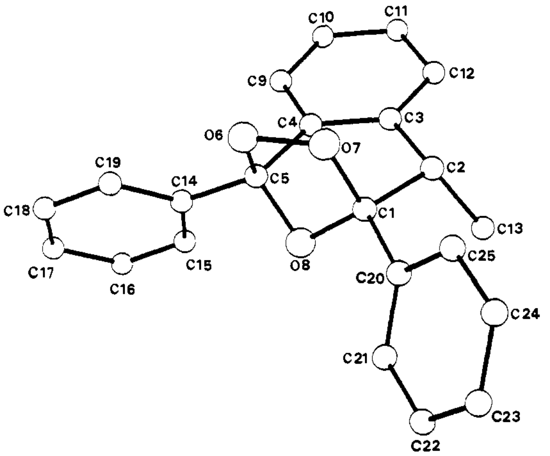


Figure 6. Molecular structure of ozonide (**2b**) as determined by X-ray analysis. The disordered atoms (**2b′**) and hydrogen atoms have been omitted.

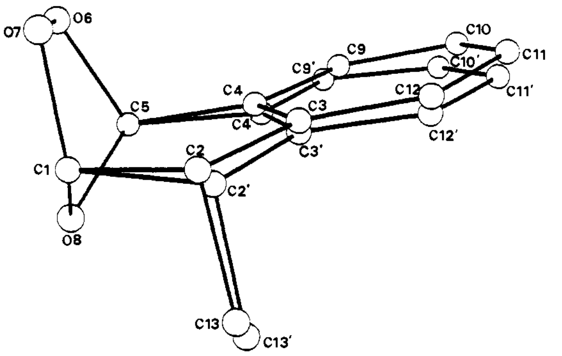


Figure 7. Disorder in the bicyclic moiety of ozonide (**2b**). The phenyl groups at C1 and C5 have been omitted.

Figure 6;[23] the numbering system is analogous to that of **3a**. Despite the disordered nature of the crystal structure, as discussed below, there is little doubt that the molecular structure corresponds exclusively to the exo isomer in which the methyl group at C2 is syn to the bridging epoxide oxygen atom (O8).

The structural refinement of ozonide **2b** did not proceed smoothly as that of the ozonide **3a**. A persistently high *R* factor ($R > 0.13$) together with unreasonable geometrical and thermal parameters suggested a disordered crystal structure. Inspection of a difference Fourier map cofirmed that the molecule was disordered in two independent regions: around the atoms C2–C4 and C9–C12 in the bicyclic moiety, and the atoms C14–C19 of the phenyl group at C5. Surprisingly, there was not apparent disorder in the central ozonide ring atoms C1, C5, and O6–O8.

The major disorder in the bicyclic moiety was most successfully modeled as an angular displacement about the C1–C5 vector (as depicted in Figure 7) with a calculated angle of 5° between the least-square planes defined by atoms C1–C5 and C9–C12 and atoms C1, C2′–C4′, C5, and C9′–C12′, respectively. Such a disorder could possibly arise from the molecule having two similarly populated conformations which pivot about the C1–C5 vector or from random improper crystal packing. Molecular models of **2b** suggest that the bicyclic skeleton is rigid and consequently would not readily accomodate the "observed" angular displacement. Furthermore, a disordered crystal packing by such a rigid system would certainly result in alternative positions for the oxygen atoms of the ozonide ring or, at least, large temperature factors associated with these atoms. In fact, the temperature factors for atoms O6–O8 and the geometrical parameters of the ozonide ring turn out to be fairly reasonable in the circumstances. Therefore, the precise nature of the disorder in this position of the molecule is as yet clear.

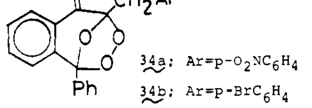
A high degree of rotational freedom about the C5–C14 bond most probably accounts for the disorder in the phenyl group at C5 in **2b**. The corresponding phenyl group in ozonide **3a** appears to have a lesser degree of rotational freedom since only the thermal parameters of atoms C16–C18 give any indication of positional uncertainty. The other phenyl group at C1 in ozonide **2b** adopts a single conformation which presumably minimizes steric interactions with the adjacent methyl group at C2.

Table XI. Corresponding Bond Distances (with ESD's) for Ozonides 3a and 2b

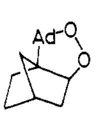
3a		2b			
bond	Å	bond	Å	bond	Å
C1–O7	1.446 (4)	C1–O7	1.48 (1)		
C1–O8	1.407 (4)	C1–O8	1.42 (1)		
O6–O7	1.469 (3)	O6–O7	1.46 (1)		
C5–O6	1.439 (3)	C5–O6	1.45 (1)		
C5–O8	1.427 (3)	C5–O8	1.43 (1)		
C1–C2	1.510 (5)	C1–C2	1.52 (1)	C1–C2′	1.52 (1)
C2–C3	1.522 (4)	C2–C3	1.52 (3)	C2′–C3′	1.52 (3)
C2–C13	1.533 (5)	C2–C13	1.56 (3)	C2′–C13′	1.56 (2)
C4–C5	1.511 (4)	C4–C5	1.53 (1)	C4′–C5	1.51 (1)
C5–C14	1.501 (4)	C5–C14	1.51 (1)	C5–C14′	1.53 (2)
C3–C9	1.391 (5)	C3–C9	1.40 (2)	C3′–C9′	1.40 (2)
C3–C4	1.392 (4)	C3–C4	1.40 (3)	C3′–C4′	1.40 (3)
C9–C10	1.381 (6)	C9–C10	1.40 (3)	C9′–C10′	1.40 (3)
C10–C11	1.365 (6)	C10–C11	1.40 (3)	C10′–C11′	1.40 (3)
C11–C12	1.379 (5)	C11–C12	1.40 (2)	C11′–C12′	1.40 (2)
C4–C12	1.387 (4)	C4–C12	1.40 (2)	C4′–C12′	1.40 (3)
C14–C15	1.373 (5)	C14–C15	1.40 (2)	C14′–C15′	1.40 (2)
C15–C16	1.391 (5)	C15–C16	1.40 (2)	C15′–C16′	1.40 (2)
C16–C17	1.357 (7)	C16–C17	1.40 (3)	C16′–C17′	1.40 (3)
C17–C18	1.373 (6)	C17–C18	1.40 (2)	C17′–C18′	1.40 (2)
C18–C19	1.380 (5)	C18–C19	1.40 (2)	C18′–C19′	1.40 (2)
C14–C19	1.378 (5)	C14–C19	1.40 (3)	C14′–C19′	1.40 (3)
		C1–C20	1.513 (10)		
		C20–C21	1.395 (6)		
		C21–C22	1.395 (9)		
		C22–C23	1.395 (7)		
		C23–C24	1.395 (6)		
		C24–C25	1.395 (9)		
		C20–C25	1.395 (7)		

The bond distances and angles for ozonides **3a** and **2b** are listed in Tables XI and XII, respectively. In general, the geometrical parameters are within expected ranges for both molecules even though they are not so precisely determined for **2b** because of the structural disorder.

The observed O–O bond lengths in **3a** and **2b** [1.469 (3) and 1.46 (1) Å] are in reasonable agreement with the values reported for the ozonides **34a** and **34b**,[24] the five-membered ring peroxide **35**,[25] and the six- and nine-membered ring ketone peroxides **36**[26] though significantly shorter than the value of 1.501 (2) Å found for the O–O bond distance in the bicyclic peroxide **37**.[27] The C–O (peroxide) distances in **3a** [1.446 (4) and 1.439 (3) Å] are



34a: Ar=p-$O_2NC_6H_4$
34b: Ar=p-BrC_6H_4



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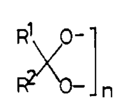

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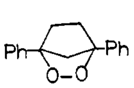

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(24) (a) Karban, J.; McAtee, J. L.; Belew, J. S.; Mullica, D. F.; Milligan, W. O.; Korp, J. *J. Chem. Soc., Chem. Commun.* **1978**, 729. (b) Mullica, D. F.; Korp, J. D.; Milligan, W. O.; Belew, J. S.; McAtee, J. L.; Karban, J. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1703. (c) Oliver, J. D.; Mullica, D. F.; Milligan, W. O.; Karban, J.; McAtee, J. L.; Belew, J. S. *Acta Crystallogr., Sect. B* **1979**, *B35*, 2276.

(25) Hitchcock, P. B.; Beheshti, I. *J. Chem. Soc., Perkin Trans. 2* **1979**, 126.

(26) Groth, P. *Acta Chem. Scand.* **1969**, *23*, 1311.

(27) Langs, D. A.; Erman, M. G.; De Titta, G. T.; Coughlin, D. J.; Salomon, R. G. *J. Cryst. Mol. Struct.* **1978**, *5*, 239.

Table XII. Corresponding Bond Angles (with ESD's) for Ozonides 3a and 2b

3a[a]		2b[b,d]		2b[c,d]	
angle	deg	angle	deg	angle	deg
C1–O8–C5	101.8 (2)	C1–O8–C5	102.0 (5)	C1–O8–C5	
O8–C1–O7	104.2 (2)	O8–C1–O7	103.0 (5)	O8–C1–O7	
O8–C5–O6	102.0 (2)	O8–C5–O6	100.8 (5)	O8–C5–O6	
C1–O7–O6	105.3 (2)	C1–O7–O6	105.9 (5)	C1–O7–O6	
C5–O6–O7	103.4 (2)	C5–O6–O7	102.0 (5)	C5–O6–O7	
C2–C1–O7	110.8 (3)	C2–C1–O7	104.7 (8)	C2′–C1–O7	109.4 (8)
C2–C1–O8	112.1 (3)	C2–C1–O8	121.4 (8)	C2′–C1–O8	105.7 (7)
C14–C5–O8	109.0 (2)	C14–C5–O8	109.1 (8)	C14′–C5–O8	109.6 (8)
C4–C5–O6	109.8 (2)	C4–C5–O6	105.8 (8)	C4′–C5–O6	116.4 (8)
C4–C5–O8	109.9 (2)	C4–C5–O8	106.8 (8)	C4′–C5–O8	116.3 (8)
C14–C5–O6	108.8 (2)	C14–C5–O6	111.2 (8)	C14′–C5–O6	101.5 (8)
C1–C2–C3	109.3 (3)	C1–C2–C3	104.0 (1)	C1–C2′–C3′	110.0 (1)
C2–C3–C4	119.6 (3)	C2–C3–C4	118.0 (1)	C2′–C3′–C4′	127.0 (1)
C3–C4–C5	118.6 (2)	C3–C4–C5	125.0 (1)	C3′–C4′–C5	107.0 (1)
C1–C2–C13	110.6 (3)	C1–C2–C13	111.0 (1)	C1–C2′–C13′	111.0 (1)
C3–C2–C13	114.0 (3)	C3–C2–C13	110.0 (1)	C3′–C2′–C13′	112.0 (1)
C2–C3–C9	122.1 (3)	C2–C3–C9	118.0 (2)	C2′–C3′–C9′	119.0 (1)
C5–C4–C12	121.6 (3)	C5–C4–C12	119.0 (1)	C5–C4′–C12′	123.0 (1)
		C20–C1–O7	107.4 (5)	C20–C1–O7	
		C20–C1–O8	109.0 (5)	C20–C1–O8	
		C20–C1–C2	110.2 (8)	C20–C1–C2′	120.9 (8)

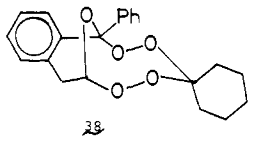
[a] Mean internal angle around (i) benzo moiety (C4, C3, C9–C12) 120 (1)°, (ii) phenyl ring (C14–C19) 120.0 (6)°. [b] Mean internal angle around benzo moiety (C4, C3, C9–C12) 120 (2)°. [c] Mean internal angle around benzo moiety (C4′, C3′, C9′–C12′) 120 (6)°. [d] Phenyl groups treated as rigid hexagons (d_{c-c} = 1.395 Å).

similar to values of around 1.44 Å reported by Groth for the ketone peroxides (**36**, *n* = 2).[26] Although C1–O7 distance in **2b** [1.48 (1) Å] is greater than **36** from 1.44 Å,[28] it is similar to the mean value of 1.47 Å observed for the corresponding distances in ozonides **34a** and **34b**.[24] These differences may be attributable to the variation in substitution at the bridgehead carbon atoms C1 and C5; ozonides **2b**, **34a**, and **34b** are fully substituted at these positions. The C–O (epoxide) bond distances exhibit good agreement with previous results.[24,29] The mean internal angle around the ozonide ring was 103° [cf. 104° for **34a** and **34b**[24]]. Least-squares mean planes[30] calculated through the atoms C2–C5 and C9–C12 of ozonide **3a** were consistent with a high degree of planarity in this region of the molecule; the maximum out-of-plane deviation was 0.05 Å. The maximum deviation from the plane defined by atoms C1–C5 and C9–C12 in ozonides **3a** and **2b** was 0.08 Å.

An important structural aspect of this study is the conformation of the respective ozonide rings in **3a** and **2b**. In each case the five-membered ring adopts a slightly distorted epoxide oxygen envelope conformation. Calculated ring puckering coordinates[31] (q_2 = 0.438 Å, ϕ_2 = 347° for **3a**; q_2 = 0.468 Å, ϕ_2 = 338° for **2b**)[32] are in accord with this deduction. The major deviations from the pure envelope geometry arise from the noncoplanarity of C5–O6–O7–C1 linkage; the C5–O6–O7–C1 torsion angles in **3a** and **2b** were −10° and −19°, respectively. These are substantially greater than the corresponding torsion angle in **34a** but of the similar magnitude to that in **34b**. The least-squares planes defined by the atoms C1, O7, O6, and C5 and C1, O8, and C5 intersect at angles of 45.7° in **3a** and 46.5° in **2b** similar to that in **34a**.

This structural study has demonstrated unambiguously that the compounds **3a** and **2b** are the endo and exo ozonides, respectively. Equilibration of these respective exo/endo pairs in the presence of a suitable Lewis acid results in the exo isomer being the major component (~7:3) of the equilibrium mixture in each case yet the two crystal structures display only minor differences around the ozonide ring. Indeed the geometrical parameters, in particular the O–O and C–O bond distances, of **3a** are more closely related to those of the thermally stable tetraoxane (**36**, *n* = 2).[26] Moreover, our results suggest that, although the five-membered rings in **3a** and **2b** are constrained to adopt pseudoenvelope conformations, these compounds are less highly strained than the endoperoxide **37**.[27]

In addition to acid-catalyzed equilibration, these ozonides undergo ring expansion under the appropriate conditions to produce pentaoxabicyclo[5.3.1]undecanes (Scheme VII and Table VII).[9] X-ray structural analysis of one crystalline derivative **38**



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indicates that the angle at the bridging oxygen is 118.0 (5)° which is substantially greater than the values of 101.8 (2)° and 102.0 (5)° in **3a** and **2b**.[33] Thus, the relief of compressional angle strain at the bridging oxygen on opening of the ozonide ring may provide some driving force for the ring expansion reaction. Nonetheless, compression of this angle C1–O8–C5 cannot be very energetically demanding since, in the first place, ozonides are readily produced by the reaction of ozone with an indene, and the five-membered ring is re-formed in the equilibration process.

Experimental Section

General Procedure. ^{1}H NMR spectra were obtained with a JNM P-S-100 spectrometer in $CDCl_3$. MS data were obtained with a Hitachi RMU-6H spectrometer and infrared spectra with a Hitachi 215 spectrometer. Ozonlyses were carried out with a Nippon Ozone Model 0-1-2 ozonator; dry oxygen containing about 2% ozone was introduced at a speed of 50 L/h in the solution of a substrate in CCl_4 at 20 °C.

Ozonolysis of 1-Methylindenes. **1a** (5 mmol) was ozonized in CCl_4 (15 mL) by passing 1 equiv of ozone through the solution. The mixture was poured onto aqueous $NaHCO_3$ and extracted with ether. The products were separated by column chromatography on silica gel. Elution with benzene–petroleum ether (1:1) gave a mixture of the corresponding isomeric ozonides **2a** and **3a** (910 mg, 72%); **2a** was a solid: mp 127–128 °C (from methanol); ^{1}H NMR δ 1.46 (d, *J* = 7.5 Hz, 3 H), 3.12 (q, *J* = 7.5 Hz, 1 H), 5.96 (br s, 1 H). Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.52; H, 5.55. Found: C, 75.42; H, 5.42. The endo ozonide **3a** was a solid: mp 151–152 °C (from methanol); ^{1}H NMR δ 1.46 (d, *J* = 7.5 Hz, 3 H), 3.52 (qxd, *J* = 7.5 and 2.6 Hz, 1 H), 5.96 (d, *J* = 2.6 Hz, 1

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(28) The microwave study of ethylene ozonide has revealed that the C–O bond (proxide) length is as short as 1.395 (6) Å; (a) Mazur, S.; Kuczkowski, R. L. *J. Mol. Spectrosc.* **1977**, *65*, 84. (b) Cremer, D. *J. Chem. Phys.* **1979**, *70*, 1898.

(29) (a) Grand, A.; Cadet, J. *Acta Crystallogr., Sect. B* **1978**, *B34*, 1524. (b) McConnell, J. F.; Stevens, J. D. *Cryst. Struct. Comm.* **1973**, *2*, 619.

(30) All least-squares planes were calculated with GEOM. Details of least squares are given in Table XV which is available as supplementary material.

(31) Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354.

(32) ϕ = 0 or 180° indicates a pure envelope conformation.

(33) McCullough, K. J.; Walkinshaw, M. D.; Nojima, M. *J. Chem. Res.* **1981**, (M), 4357–4370; (S), 369.

H). Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.52; H, 5.55. Found: C, 75.48; H, 5.50.

From the second fraction [elution with benzene–petroleum ether–ether (50:50:3)], 1-methyl-3-phenyl-2-indanone was obtained as an oil (a mixture of cis and trans forms, cis:trans ratio = 1:2); IR (neat) 1750 cm^{-1}, NMR δ 1.45 (d, J = 7.5 Hz, CH_3 of the cis isomer), 1.47 (d, J = 7.5 Hz, CH_3 of the trans isomer), 3.66 (q, J = 7.5 Hz, C*H*CH_3), 4.70 (s, C*H*C_6H_5 of the trans isomer), 4.73 (s, C*H*C_6H_5 of the cis isomer). The ozonides **2a** and **3a** were separated by column chromatography on silica gel using benzene–petroleum ether (1:4).

From the ozonlyses of 1-methylindenes **1b–d** were obtained the corresponding mixtures of the exo and endo ozonides **2b–d** and **3b–d**. Exo ozonide **2b** was a solid: mp 125–126 °C (from methanol); NMR δ 1.20 (d, J = 7.5 Hz, 3 H), 3.60 (q, J = 7.5 Hz, 1 H). Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 80.15; H, 5.14. Endo ozonide **3b** was a solid: mp 136–137 °C (from methanol); NMR δ 1.38 (d, J = 7.5 Hz, 3 H), 3.90 (q, J = 7.5 Hz, 1 H). Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.90; H, 5.33. Exo ozonide **2c** was a solid: mp 134–135 °C (from methanol); NMR δ 1.09 (d, J = 7.5 Hz, 3 H), 2.09 (s, 3 H), 3.47 (q, J = 7.5 Hz, 1 H). Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.28; H, 5.93. Endo ozonide **3c** was a solid: mp 68–69 °C (from methanol); NMR δ 1.28 (d, J = 7.5 Hz, 3 H), 1.98 (s, 3 H), 3.71 (q, J = 7.5 Hz, 1 H). Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.22; H, 5.77. Exo ozonide **2d** was a solid: mp 110–111 °C (from methanol); NMR δ 1.32 (d, J = 7.5 Hz, 3 H), 1.98 (s, 3 H), 2.98 (q, J = 7.5 Hz, 1 H), 5.80 (s, 1 H). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.33; H, 6.20. Endo ozonide **3d** was a solid: mp 73–75 °C (from methanol); NMR δ 1.32 (d, J = 7.5 Hz, 3 H), 1.98 (s, 3 H), 3.33 (qxd, J = 7.5 and 2.6 Hz, 1 H), 5.80 (d, J = 2.6 Hz, 1 H). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 69.06; H, 6.27.

Configurations of **2a** and **3a** were assigned as described in the text. We assigned one isomeric 1,3-dimethylindene ozonide, whose C2 hydrogen resonanced at a higher magnetic field (δ 2.98), as *exo*-**2d** and another isomer (δ 3.33) as *endo*-**3d**, on the basis of the same relation in chemical shift between the C2 hydrogen of **2a** and that of **3a**. This relation in chemical shift was used to assign other stereoisomeric ozonides. X-ray study for **2b** supported the above assignment.

Reaction of Ozonides in the Presence of $ClSO_3H$ in AcOH. To a solution of 1-methyl-3-phenylindene ozonide (a 3:2 mixture of **2a** and **3a**, 3 mmol) in acetic acid–methylene chloride (55 mL, 8:3 v/v) was added a solution of $ClSO_3H$ in CH_2Cl_2 (5 mL) in one portion, and the mixture was kept with stirring at 20 °C for 44 h. After conventional workup the neutral products were isolated by column chromatography on silica gel using 8:10:82 ether–benzene–petroleum ether. The first fraction contained a mixture of **2a** and **3a** (12%), the **2a**/**3a** ratio being 7:3. From the second fraction was isolated 1-(2-benzoyloxyphenyl)propionaldehyde (**4a**) in 11% yield: an oil; NMR δ 1.32 (d, J = 7.5 Hz, 3 H), 3.71 (q, J = 7.5 Hz, 1 H), 7.20–8.22 (m, 9 H), 9.69 (s, 1 H); IR 1735, 1720, 1260, 1210, 1170, 1060, 1020 cm^{-1}. The reaction of **4a** with *p*-toluenesulfonyl hydrazide in ethanol gave the corresponding hydrazone as a white solid: mp 127–130 °C (from ethanol); IR 1490, 1450, 1260, 1200, 1140, 1100, 1005 cm^{-1}. Anal. Calcd for $C_{23}H_{22}N_2O_4S$: C, 65.39; H, 5.25; N, 6.63; S, 7.59. Found: C, 65.05; H, 5.22; N, 6.46; S, 7.65. Treatment of **4a** with KOH in aqueous ethanol gave, together with benzoic acid, 1-(2-hydroxyphenyl)propionaldehyde: an oil; IR 3300, 1720 cm^{-1}. The third fraction gave 1-(2-benzoylphenyl)propionaldehyde (**7a**) in 18% yield: an oil; NMR δ 1.35 (d, J = 7.5 Hz, 3 H), 3.92 (q, J = 7.5 Hz, 1 H), 6.90–7.90 (m, 9 H), 9.60 (s, 1 H); IR 1700, 1660 cm^{-1}. From the final fraction was obtained 2-(2-benzoyloxyphenyl)-2-methylethenol (**5a**): a solid; mp 91–92 °C (from methanol); mass spectrum, *m/e* 254 (M^+); NMR δ 2.01 (s, 3 H), 5.28 (s, 1 H), 6.90–7.95 (m, 10 H); IR 3500, 1720, 1280, 1150 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.30; H, 5.47. From the acid layer was obtained 1-(2-benzoylphenyl)propionic acid (**6a**): mp 86–87 °C (from CCl_4–petroleum ether); IR 3200, 1700, 1660 cm^{-1}: NMR δ 1.67 (d, J = 7.5 Hz, 3 H), 4.09 (q, J = 7.5 Hz, 1 H), 7.00–8.00 (m, 9 H). Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.59; H, 5.55. Found: C, 75.06; H, 5.51.

The reaction of a mixture of **2b** and **3b** (**2b**/**3b** = 2:3) gave a mixture of **4b**, **5b**, and **7b**. The rearranged product **4b** was an oil: NMR δ 1.48 (d, J = 7.5 Hz, 3 H), 4.80 (q, 7.5 Hz, 1 H), 7.20–8.31 (m, 14 H); IR 1730, 1680, 1250, 1205, 1060 cm^{-1}. Hydrolysis of **4b** with KOH in aqueous ethanol gave, along with benzoic acid, 1-(2-hydroxyphenyl)ethyl phenyl ketone: mp 105–106 °C (from methanol); NMR δ 1.55 (d, J = 7.5 Hz, 3 H), 4.89 (q, J = 7.5 Hz, 1 H), 6.70–8.10 (m, 10 H); IR 3300, 1665 cm^{-1}. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 78.99; H, 6.23. The ethenol **5b** was obtained as an oil: mass spectrum, *m/e* 330 (M^+); NMR δ 2.13 (s, 3 H), 6.75–8.34 (m, 15 H); IR 3400, 1730, 1270, 1130 cm^{-1}. Hydrolysis of **5b** with KOH in aqueous ethanol gave a mixture of benzoic acid and 1-(2-hydroxyphenyl)ethyl phenyl ketone. 1-(2-Benzoylphenyl)ethyl phenyl ketone (**7b**) was a solid: mp 107 °C (from methanol); NMR δ 1.45 (d, J = 6.0 Hz, 3 H), 5.12 (q, J = 6.0 Hz, 1 H), 7.30–8.00 (m, 14 H); IR 1680, 1660 cm^{-1}.

The reaction of **2c** gave **4c**: an oil; mass spectrum, *m/e* 328 (M^+); NMR δ 1.36 (d, J = 7.5 Hz, 3 H), 2.24 (s, 3 H), 4.50 (q, J = 7.5 Hz, 1 H), 6.87–7.90 (m, 9 H); IR 1760, 1680 cm^{-1}. Hydrolysis of **4c** with KOH in aqueous ethanol gave a mixture of benzoic acid and 1-(2-hydroxyphenyl)ethyl phenyl ketone. From **2d** was obtained **6d**: mp 103–105 °C (from benzene–petroleum ether); IR 3400, 1720, 1680 cm^{-1}.

Reaction of Ozonides in the Presence of $ClSO_3H$ in CH_2Cl_2. A solution of $ClSO_3H$ (1.0 mmol) in CH_2Cl_2 (5 mL) was added to a solution of **2a** and **3a** (10 mmol, **2a**/**3a** = 3:2) in CH_2Cl_2 in one portion, and the reaction was continued for a further 3 h at 20 °C. The products were treated as above.

Methanolysis of Ozonides in the Presence of $ClSO_3H$. To a solution of an ozonide (1 mmol) in methanol (10 mL) was added a solution of $ClSO_3H$ in CH_2Cl_2 (3 mL) in one portion, and the mixture was kept with stirring at 20 °C for 4 h. After conventional workup the neutral products were isolated by column chromatography on silica gel. 4,5-Dihydro-1,4-dimethoxy-1-phenyl-4-methyl-1*H*-2,3-benzodioxepin (**15a**) was a solid: mp 92–94 °C (from methanol); NMR δ 1.42 (d, J = 6.0 Hz, 3 H), 3.45 (s, 3 H), 3.54 (s, 3 H), 3.82 (qxd, J = 6.0 and 8.0 Hz, 1 H), 4.46 (d, J = 8.0 Hz, 1 H), 7.20–7.82 (m, 9 H); IR 1190, 1140, 1090, 1070, 975 cm^{-1}. 2-(2,2-Dimethoxy-1-methylethyl)benzophenone (**16a**) was an oil: NMR δ 1.19 (d, J = 7.5 Hz, 3 H), 3.09 (s, 3 H), 3.15 (s, 3 H), 3.35 (qxd, J = 7.5 and 6.0 Hz, 1 H), 4.28 (d, J = 6.0 Hz, 1 H), 7.04–7.84 (m, 9 H); IR 1660, 1280, 1060 cm^{-1}. Methyl 1-(2-benzoylphenyl)propionate (**17a**) was an oil: NMR δ 1.50 (d, J = 7.5 Hz, 3 H), 3.51 (s, 3 H), 4.14 (q, J = 7.5 Hz, 1 H), 7.20–7.90 (m, 9 H); IR 1740, 1660, 1280, 1260, 1060, 920 cm^{-1}.

The hemiperacetal **15d** was an oil: NMR δ 1.39 (d, J = 7.5 Hz, 3 H), 1.41 (s, 3 H), 3.20 (s, 3 H), 3.26 (s, 3 H), 3.57 (qxd, J = 7.5 and 7.5 Hz), 4.21 (d, J = 7.5 Hz, 1 H), 7.15–8.48 (m, 4 H); IR 2950, 1460, 1260, 1150, 1090, 980 cm^{-1}.

Investigation of the Reaction of Ozonides in the Presence of $ClSO_3H$ by NMR Spectroscopy. The samples were prepared for NMR analysis in the 5-mm NMR tubes by the addition of a solution of $ClSO_3H$ (0.02 mmol) in $CDCl_3$ (0.5 mL) to a solution of an ozonide (0.2 mmol) in acetic-d_3 acid-*d* (0.5 mL), and the NMR spectra were recorded periodically at 20 °C. In the reaction with methanol, methanol-d_4 (0.5 mL) was used in place of acetic-d_3 acid-*d*. The decrease in the amount of ozonide and increase in the amount of products was estimated by comparing the intensities of their characteristic peaks.

Hydrogen–Deuterium Exchange on the Bridgehead Methyl of the Ozonides 2c,d. To a solution of **2d** (0.5 mmol) in CD_3OD–$CDCl_3$ (1 mL, 1:1 v/v) was added a solution of $ClSO_3H$ (0.05 mmol) in $CDCl_3$ (0.5 mL) in one portion, and the mixture was kept with stirring at 20 °C for 5 h. After conventional workup the neutral products were chromatographed on silica gel to afford deuterated ozonide (50%). The NMR and mass spectra revealed that 66% of the hydrogens of the bridgehead methyl of **2d** were replaced by deuterium. When the reaction of **2c** was performed for 1 h under the same conditions, there was recovered 30% of **2c**, in which 33% of the hydrogens of the bridgehead methyl were replaced by deuteriums. The reaction of **2d** in a solution in $CDCl_3$–acetic-d_3 acid-*d* (1:1 v/v) for 2 h resulted in the recovery of 60% of **2d**, 85% of the hydrogens of the bridgehead methyl being replaced by deuteriums. From the reaction of **2c** in acetic-d_3 acid-*d* for 1 h, was isolated 25% of **2c**, 44% of the hydrogens of the bridgehead methyl being replaced by deuteriums.

Reaction of 2a and 3d with $AlHCl_2$. To anhydrous $AlCl_3$ (12 mmol) was added anhydrous ether (40 mL) at 0 °C, followed by 4 mmol of $LiAlH_4$. To this solution was added a solution of **2a** (2 mmol) in ether (40 mL) in 5 min. The mixture was kept at 0 °C for 15 min, and then the reaction was continued at 20 °C for a further 45 min. The products were chromatographed on silica gel. Elution with petroleum ether–benzene (4:1) gave 1-phenyl-4-methyl-1*H*-2-benzopyran in 25% yield: an oil; NMR δ 1.89 (s, 3 H), 6.00 (s, 1 H), 6.46 (br s, 1 H), 6.40–7.50 (m, 9 H); IR 1645, 1150, 1130 cm^{-1}. From the second fraction was obtained 2% of *trans*-3,4-dihydro-1-phenyl-4-methyl-1*H*-2-benzopyran: an oil; mass spectrum, *m/e* 224 (M^+); NMR δ 1.26 (d, J = 7.5 Hz, 3 H), 3.01 (qxt, J = 7.5 and 7.5 Hz, 1 H), 3.41 (dxd, J = 7.5 and 12.0 Hz, 1 H), 3.95 (dxd, J = 7.5 and 12.0 Hz, 1 H), 5.61 (s, 1 H), 6.56–7.32 (m, 9 H). The third fraction contained *cis*-3,4-dihydro-1-phenyl-4-methyl-1*H*-2-benzopyran (42%): mp 54–57 °C (from methanol); *m/e* 224 (M^+); NMR δ 1.39 (d, J = 7.5 Hz, 3 H), 2.81 (qxt, J = 7.5 and 3.0 Hz, 1 H), 3.75 (dxd, J = 12.0 and 3.0 Hz, 1 H), 3.87 (dxd, J = 12.0 and 3.0 Hz, 1 H), 5.51 (s, 1 H), 6.54–7.35 (m, 9 H); IR 1120 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.10. Found: C, 85.54; H, 7.27 (for the assignment of the configuration, see below). Elution with methanol gave the diol **24a** in 30% yield. The physical properties of the acetate from

24a were the same with those of the acetate obtained by the reaction of **2a** with $LiAlH_4$, followed by acetolysis.

The reaction of **3d** with $AlHCl_2$ gave two 3,4-dihydro-1*H*-2-benzopyrans. *cis*-3,4-Dihydro-1,4-dimethyl-1*H*-2-benzopyran was an oil: mass spectrum, *m/e* 162 (M^+); NMR δ 1.21 (d, J = 7.5 Hz, 3 H), 1.49 (d, J = 6.0 Hz, 3 H), 2.78 (qxd, J = 7.5 and 3.0 Hz, 1 H), 3.83 (d, J = 3.0 Hz, 2 H), 4.76 (q, J = 6.0 Hz, 1 H), 6.96–7.32 (m, 4 H). The trans isomer was an oil: mass spectrum, *m/e* 162 (M^+); NMR δ 1.33 (d, J = 7.5 Hz, 3 H), 1.49 (d, J = 6.0 Hz, 3 H), 3.05 (qxt, J = 7.5 and 7.5 Hz, 1 H), 3.41 (dxd, J = 7.5 and 12.0 Hz, 1 H), 4.07 (dxd, J = 7.5 and 12.0 Hz, 1 H), 4.76 (q, J = 6.0 Hz, 1 H), 6.96–7.32 (m, 4 H).

Reaction of 2a,d with $AlDCl_2$: Assignment of the Configuration of the Products. The reaction of **2a** with $AlDCl_2$ gave, along with 1-phenyl-4-methyl-1*H*-benzopyran-*1-d* (**23**) and dideuterated **24a**, four 3,4-dihydro-1*H*-2-benzopyrans. Column chromatography of the latter products on silica gel gave two fractions in a ratio of 1:9. The NMR spectrum of the first (minor) fraction showed that the signals attributable to the hydrogens at the 3-position appear at δ 3.37 (d, J = 7.5 Hz) and 3.90 (d, J = 7.5 Hz), the ratio of the peak areas being 2:3. In the case of the second fraction, the hydrogens at the same position appeared at δ 3.87 (d, J = 3.0 Hz) and 3.75 (d, J = 3.0 Hz), the ratio being 7:3. On the basis of Karplus theory, conformations **19a** and **20a** were considered to require a smaller coupling constant, and inversely, a larger coupling constant was expected for conformations **21a** and **22a**. Thus, the first fraction was determined to be a mixture of **21a** and **22a** and the second a mixture of **19a** and **20a**. By the application of a well-established empirical rule that in cyclohexane system an equatorial proton appears in a lower field compared with the corresponding axial proton, the minor isomer and the major one of the first fraction were assigned as **21a** and **22a**, respectively. On the same basis, the major isomer and the minor one of the second fraction were assigned as **19a** and **20a**, respectively.

Reaction of **2d** with $AlDCl_2$ afforded **19d**–**22d**, which were separated into two fractions by column chromatography, i.e., a mixture of **19d** and **20d** and that of **21d** and **22d**. The NMR spectrum of the mixture of **19d** and **20d** had the following characteristics: δ 1.34 (d, J = 7.5 Hz, 3 H), 1.52 (s, 3 H), 2.77 (qxd, J = 7.5 and 3.0 Hz, 1 H), 3.86 (br d, 1 H), 7.02–8.34 (m, 4 H). For the mixture of **21d** and **22d** the following signals were observed in the NMR spectrum: δ 1.20 (d, J = 7.5 Hz, 3 H), 1.50 (s, 3 H), 3.04 (qxd, J = 7.5 and 7.5 Hz, 1 H), 3.46 (d, J = 7.5 Hz), 4.16 (d, J = 7.5 Hz), 7.02–8.34 (m, 4 H). By the comparison of the peak areas of the signals at δ 3.46 and 4.16, the **21d**/**22d** ratio was determined.

Reaction of 2b,c and 3b,c with $AlHCl_2$. The reaction of **2b** with $AlHCl_2$ gave three 3,4-dihydro-1*H*-2-benzopyrans. The NMR spectrum of the product eluted first had the following characteristics for the hydrogen at the 3-position: δ 5.12 (d, J = 3.0 Hz); the secondone, δ 4.98 (d, J = 3.0 Hz); the third one, δ 4.49 (d, J = 7.5 Hz), the ratio being 69:9:22. The possible products were **19b**–**22b**, with the phenyl substituent at the 3-position occupying the pseudoequatorial position. On the basis of Karplus theory, conformations **19b** and **21b** were supposed to require a smaller coupling constant. By the fact that **19a** was a major product from **2a**, the product eluted first was determined to be **19b** and the second one **21b**. When the higher yield of **20a** compared with **22a** was seen, the third one having a larger coupling constant was considered to be **20b** rather than **22b**. Thus, **19b**–**21b** were determined to have the following physical properties. *cis,cis*-3,4-Dihydro-1,3-diphenyl-4-methyl-1*H*-2-benzopyran (**19b**) was a solid: mp 169–171 °C (from methanol); NMR δ 1.08 (d, J = 7.5 Hz, 3 H), 3.10 (qxd, J = 7.5 and 3.0 Hz, 1 H), 5.12 (d, J = 3.0 Hz, 1 H), 5.90 (s, 1 H), 6.72–7.50 (m, 14 H); IR 1235, 1060, 1000 cm^{-1}. Anal. Calcd for $C_{22}H_{20}O$: C, 87.96; H, 6.71. Found: C, 87.36; H, 6.67. The trans,trans isomer **20b** was an oil: mass spectrum, *m/e* 300 (M^+); NMR δ 1.27 (d, J = 7.5 Hz, 3 H), 3.28 (qxd, J = 7.5 and 7.5 Hz, 1 H), 4.49 (d, J = 7.5 Hz, 1 H), 6.17 (s, 1 H), 6.60–7.60 (m, 14 H). The trans,cis isomer **21b** was a solid: mp 127–130 °C (from methanol); mass spectrum, *m/e* 300 (M^+); NMR δ 0.98 (d, J = 7.5 Hz, 3 H), 3.09 (qxd, J = 7.5 and 3.0 Hz, 1 H), 4.98 (d, J = 3.0 Hz, 1 H), 6.17 (s, 1 H), 6.95–7.47 (m, 14 H). Anal. Calcd for $C_{22}H_{20}O$: C, 87.96; H, 6.71. Found: C, 87.31; H, 6.67.

The reaction of **2c** gave two 3,4-dihydro-1*H*-2-benzopyrans **19c** and **20c**. The cis,cis isomer **19c** was an oil: mass spectrum, *m/e* 238 (M^+); IR 1320, 1110 cm^{-1}; NMR δ 0.92 (d, J = 7.5 Hz, 3 H), 1.58 (d, J = 6.0 Hz, 3 H), 2.90 (qxd, J = 7.5 and 3.0 Hz, 1 H), 4.82 (d, J = 3.0 Hz, 1 H), 4.97 (q, J = 6.0 Hz, 1 H), 6.96–7.42 (m, 9 H). The trans,trans isomer **20c** was an oil: mass spectrum, *m/e* 238 (M^+); NMR δ 0.92 (d, J = 7.5 Hz, 3 H), 1.58 (d, J = 6.0 Hz, 3 H), 2.90 (qxd, J = 7.5 and 7.5 Hz, 1 H), 5.03 (d, J = 7.5 Hz, 1 H), 5.19 (q, J = 6.0 Hz, 1 H), 6.96–7.42 (m, 9 H). From **3c** was obtained a mixture of **19c** and **21c**. The trans,cis isomer **21c** was a solid: mp 100–106 °C (from methanol); mass spectrum, *m/e* 238 (M^+); NMR δ 0.86 (d, J = 7.5 Hz, 3 H), 1.54 (d, J = 6.0 Hz, 3 H), 2.90 (qxd, J = 7.5 and 3.0 Hz, 1 H), 3.83 (d, J = 3.0 Hz, 2 H), 4.76 (q, J = 6.0 Hz, 1 H), 6.96–7.32 (m, 9 H).

Reaction with Bis(α-hydroxy-4-methylbenzyl) Peroxide (31) in the Presence of $ClSO_3H$. To a solution of **2a** (2 mmol) and **31** (2 mmol) in AcOH (15 mL) was added a solution of $ClSO_3H$ (0.2 mmol) in AcOH (5 mL) in one portion, and the reaction was continued with stirring for a further 4 h at 20 °C. After conventional workup the products were chromatographed on silica gel. Elution with 1/1 petroleum ether–benzene afforded a mixture of **2a** and **3a** (25%, the ratio 7:3). From the second fraction was obtained a mixture of **32a** and **33a**. By repeated column chromatography *exo*- (**32a**) and *endo*-8-methyl-1-phenyl-4-tolyl-9,10-benzo-2,3,5,6,11-pentaoxabicyclo[5.3.1]undecane (**33a**) were isolated in pure states. The exo isomer **32a** was a solid: mp 199–203 °C (from methanol); IR 1320, 1260, 1205, 1130, 1085, 1020, 1005, 980 cm^{-1}; NMR δ 1.55 (d, J = 7.5 Hz, 3 H), 2.35 (s, 3 H), 3.12 (q, J = 7.5 Hz, 1 H), 5.80 (s, 1 H), 6.56 (s, 1 H), 6.80–7.72 (m, 13 H). Anal. Calcd for $C_{24}H_{22}O_5$: C, 73.83; H, 5.68. Found: C, 73.53; H, 5.66. The endo isomer **33a** was a solid: mp 208–209 °C (from methanol); NMR δ 1.55 (d, J = 7.5 Hz, 3 H), 2.34 (s, 3 H), 3.60–3.80 (br s, 1 H), 5.90 (d, J = 4.5 Hz, 1 H), 6.55 (s, 1 H), 6.80–7.76 (m, 13 H). The configurations of **32a** and **33a** were assigned on the basis of Karplus theory, which suggested that the hydrogen of **32a** at the 8-position has a negligible coupling constant whereas a relatively larger one is expected in the case of **33a** reflecting the different dihedral angles with the hydrogens at the 7-position: In the case of **32a** the dihedral angle is around 90° while the corresponding dihedral angle in **33a** is around 20°.

Reaction of 2d or 3d with a Mixture of *p*-Tolualdehyde and 30% H_2O_2 in the Presence of $ClSO_3H$. The reaction of **3d** (3 mmol) with a mixture of *p*-tolualdehyde (6 mmol) and 30% H_2O_2 in the presence of $ClSO_3H$ (0.3 mmol) in AcOH (30 mL) gave, along with **2d** and **3d**, two peroxides **32d** and **33d**. The exo peroxide **32d** was a solid: mp 135–137 °C (from methanol); mass spectrum, *m/e* 328 (M^+); IR 1290, 1180, 1150, 1100, 1010 cm^{-1}; NMR δ 1.38 (d, J = 7.5 Hz, 3 H), 1.91 (s, 3 H), 2.31 (s, 3 H), 2.91 (q, J = 7.5 Hz, 1 H), 5.60 (s, 1 H), 6.29 (s, 1 H), 7.13–7.46 (m, 8 H). Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.33; H, 6.07. The endo isomer **33d** was a solid: mp 114–116 °C (from methanol); mass spectrum, *m/e* 328 (M^+); NMR δ 1.38 (d, J = 7.5 Hz, 3 H), 1.88 (s, 3 H), 2.30 (s, 3 H), 3.42 (qxd, J = 7.5 and 6.0 Hz, 1 H), 5.70 (d, J = 6.0 Hz, 1 H), 6.29 (s, 1 H), 7.05–7.40 (m, 8 H). Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.31; H, 6.04.

Structure Determination of Ozonides 3a and 2b. The intensity data from single crystals of **3a** and **2b** were collected on an Enraf-Nonius CAD4 four-circle diffractometer using Cu Kα radiation.[34] Both sets of data were corrected for Lorentz and polarization effects and crystal decay but not for absorption. For the ozonide **3a**: The systematic absences ($h0l$, $l = 2n + 1$; $0kl$, $k = 2n + 1$; and $hk0$, $h = 2n + 1$) indicated that the space group was *Pbca*. Of 1885 unique reflections collected, 1149 had $I > 2.5\sigma(I)$ where σ is the standard deviation of the background corrected count. The positions of all the non-hydrogen atoms were determined by direct methods with the program MULTAN[35] and subsequently refined with SHELX.[36] After several cycles of full-matrix least-squares refinement of the atomic coordinates and isotropic temperature factors for the carbon and oxygen atoms, the conventional R factor reduced to 0.126. Least-squares refinement was continued by using anisotropic temperature factors. The hydrogen atoms were all subsequently located on a difference Fourier map and included in the refinement process. At convergence, the conventional and weighed R factors were 0.0395 and 0.0380, respectively. The application of the weighting scheme ($W = 0.7566/[\sigma^2(F) + 0.0001(F^2)]$ was found to give satisfactory variances of $|F|$ analyzed both in ranges $|F|$ and sin θ. The final difference map showed no features greater than ± 0.15 $e^- Å^{-3}$.

For ozonide **2b**: Since the observed reflections satisfied the general conditions (hkl, $-h+k+l = 3n$), the space group $R\bar{3}$ with one molecule per asymmetric unit was indicated. Of the 2270 unique reflections measured, 1604 had $I > 2.5\sigma(I)$ and were considered observed. Application of direct methods (MULTAN[35]) revealed the positions of all the non-hydrogen atoms except one carbon atom (C17); this was subsequently located on a difference Fourier map. Although full-matrix least-squares refinement (SHELX[36]) using isotropic temperature factors for the carbon and oxygen atoms reduced the R factor to 0.14, the bond lengths and angles were outside the expected ranges and several of the temperature factors were exceptionally large. Close examination of the difference map indicated the crystal structure was disordered in two

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(34) The intensity data were collected by Dr. M. B. Hursthouse (QMC, London) through the SERC/QMC Data Collection Service.

(35) Main, P.; Woolfson, M. M.; Lessinger, L.; Germain, G.; Declerq, J. P. "MULTAN 76, a System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data", Universities of York and Louvain, 1976.

(36) Sheldrick, G. "SHELX, a System of Programs for Crystal Structure Determination", Cambridge, 1976.

regions of the molecule; around the benzo moiety and the phenyl group at C5. Separation of the disordered structures was not straightforward since several of the related disordered atoms were located within 0.5 Å of each other. Nonetheless, smooth convergence was eventually realized by constraining corresponding bond lengths to be equal within $\sigma = 0.005$ Å. The phenyl groups were treated as rigid planar groups with C–C bond lengths 1.395 Å and internal angle 120°. Only the hydrogen atoms around the nondisordered phenyl group at C1, which could be readily located on a difference Fourier map, were included in the refinement with fixed coordinates and temperature factors. The occupancy factors of the disordered structures, constrained to add to 1.0, refined to 50% in each region. This value was fixed in the final stages of structural refinement. A unit weighting scheme was found to be adequate.

When all the non-hydrogen atoms in the disordered structure were refined with individual temperature factors, the conventional R factor converged to 0.105. Further structural refinement with anisotropic temperature factors for the atoms of the ozonide ring and the phenyl group at C1, which were not evidently disordered, produced an R factor of 0.092. The final difference Fourier map contained no feature greater than ± 0.36 e$^-$ Å^{-3}.

In addition to the tabulated material already mentioned in the main text, tables of thermal vibrational parameters, calculated least-square planes, and observed and calculated structure factor amplitudes for each determination are available as supplementary material.

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Registry No. **1a**, 22360-62-9; **1b**, 51310-25-9; **1c**, 58310-20-6; **1d**, 2177-48-2; **2a**, 84810-14-0; **2b**, 84810-15-1; **2c**, 84810-16-2; **2d**, 84810-17-3; **2e**, 73258-06-7; **3a**, 84847-60-9; **3b**, 84847-61-0; **3c**, 84847-62-1; **3d**, 84847-63-2; **4a**, 84810-18-4; **4a** tosylhydrazone, 84810-19-5; **4b**, 84810-20-8; **4c**, 84810-21-9; **5a**, 84810-22-0; **5b**, 84810-23-1; **6a**, 73721-00-3; **6d**, 84810-24-2; **7a**, 84810-25-3; **7b**, 75519-83-4; **15a**, 84810-26-4; **15d**, 84810-27-5; **16a**, 84810-28-6; **17a**, 84810-29-7; **19b**, 84810-30-0; **19c**, 84810-31-1; **19d**, 84810-32-2; **20b**, 84810-33-3; **20c**, 84810-34-4; **20d**, 84810-35-5; **21b**, 84810-36-6; **21c**, 84810-37-7; **21d**, 84810-38-8; **22d**, 84810-39-9; **31**, 77196-47-5; **32a**, 84810-40-2; **32d**, 84810-41-3; **33a**, 84847-64-3; **33d**, 84847-65-4; $ClSO_3H$, 7790-94-5; $SbCl_5$, 7647-18-9; *cis*-1-methyl-3-phenylindanone, 84810-42-4; *trans*-1-methyl-3-phenylindanone, 84810-43-5; 2-(2-hydroxyphenyl)propionaldehyde, 84810-44-6; 1-(2-hydroxyphenyl)ethyl phenyl ketone, 84810-45-7; 1-phenyl-4-methyl-1*H*-2-benzopyran, 50431-53-3; *trans*-3,4-dihydro-1-phenyl-4-methyl-1*H*-2-benzopyran, 84810-46-8; *cis*-3,4-dihydro-1-phenyl-4-methyl-1*H*-2-benzopyran, 84810-47-9; *cis*-3,4-dihydro-1,4-dimethyl-1*H*-2-benzopyran, 84810-48-0; *trans*-3,4-dihydro-1,4-dimethyl-1*H*-2-benzopyran, 84810-49-1.

Supplementary Material Available: The listing of thermal vibrational parameters, calculated least-squares mean planes, and the observed and calculated structure factors for **3a** and **2b** (19 pages). Ordering information is given on any current masthead page.

Synthesis, Molecular Structure, and Chemistry of (p)-[(Tris(2-aminoethyl)amine)(2-(dihydroxymethyl)glycinate)]cobalt(III)–Zinc Tetrachloride–Water[1]

W. G. Jackson,* G. M. McLaughlin, A. M. Sargeson,*† and A. D. Watson

Contribution from the Chemistry Department, Faculty of Military Studies, University of New South Wales, Royal Military College, Duntroon A.C.T., 2600 Australia, and the Research School of Chemistry, The Australian National University, Canberra A.C.T., 2600 Australia.

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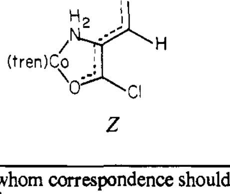
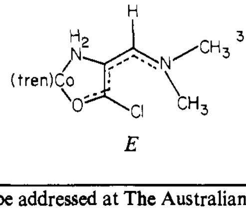
Abstract: The synthesis of chelated *C*-formylglycinate ion is described using the Vilsmeier–Haack adduct derived from the (p)-[Co(tren)glycinato]$^{2+}$ ion (tren = tris(2-aminoethyl)amine). The aldehyde hydrates readily in water, and an X-ray crystallographic study has established the structure of the hydrated formyl glycine residue and determined the overall stereochemistry of the complex. The aldehyde also equilibrates rapidly with the hydrate in water and tautomerizes to the enamine and to the imine. The last leads to proton exchange on the formyl group. The aldehyde is reduced readily with BH_4^- to the serinato complex and adds alcohols to give the hemiacetal.

Introduction

Recently[2] we described the reaction between the Vilsmeier reagent $POCl_3$/dimethylformamide and the activated methylene group of chelated glycine in (p)-[Co(tren)($NH_2CH_2CO_2$)]$^{2+}$. The remarkably stable iminium derivative (p)-[Co(tren)$NH_2C(CH{\cdot}N(CH_3)_2)CO(Cl)$]$ZnCl_4{\cdot}Cl{\cdot}2H_2O$ (*Z* isomer) was obtained in ≥80% yield. Evidence was presented for the existence of a small amount of the unstable *E* isomer, which appeared to hydrolyze rapidly to the aldehyde complex (p)-[Co(tren)$NH_2CH(CHO)CO_2$]$^{2+}$. We now report an efficient synthesis of chelated formylglycine from the major Vilsmeier product (*Z*) and some reactions of this aldehyde.[1] The protected formylglycine is a key intermediate in the laboratory synthesis of penicillin,[3] and the tetraaminecobalt(III)-protected molecules (particularly the chiral derivatives) are useful precursors to these and other natural products that we will report upon later.



Z



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† To whom correspondence should be addressed at The Australian National University.

(1) tren = tris(2-aminoethyl)amine; p and t refer to the geometric isomers where the oxygen of the substituted glycine ligand is trans to a primary (p) nitrogen or the tertiary (t) nitrogen of the tren ligand.

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