2932 J. Am. Chem. Soc. 1984, 106, 2932-2936

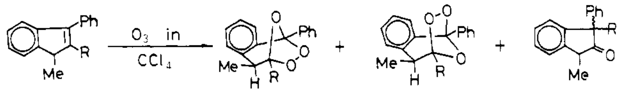
Ozonolysis of a Series of 1-Substituted Indenes. The Substituent Steric Effects on the Ozonide Exo/Endo Ratios

Masahiro Miura,[1a] Masatomo Nojima,*[1a] Shigekazu Kusabayashi,[1a] and Kevin J. McCullough*[1b]

Contribution from the Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan, and the Department of Chemistry, Heriot-Watt University, Edinburgh EH14 4AS, Scotland. *Received October 11, 1983. Revised Manuscript Received January 13, 1984*

Abstract: The ozonolysis of a series of disubstituted (1,2 and 1,3) and trisubstituted (1,2,3) indenes **1–28** in carbon tetrachloride at 20 °C has been investigated. The major product in each case was the corresponding bicyclic ozonide, usually obtained as a mixture of exo and endo isomers, whose ratio varied markedly, but inconsistently, with the nature of the 1- and 2-substituents. Since the product stereochemistry was found to show little dependence on the relative isomer stability or the substituent electronic effects, the results have been discussed in terms of the direction of approach of the ozone to the indene substrate.

Recent experimental and theoretical studies on ozonolysis of alkenes have been directed toward understanding the nature of the key intermediate carbonyl oxide (peroxymethylene) and the mechanism of 1,3-dipolar addition and reversion in the three-step Criegee mechanism.[2-4] To this end analysis of the cis/trans ratios of product ozonides (1,2,4-trioxolanes) has provided important insight. During our continuing research on the acidolysis of ozonides,[5] we were interested in the preparation of another pair of stereoisomers, namely the exo/endo ozonides derived from the ozonolysis of some 1-methylindenes.[6] The reaction of 1-methyl-3-phenylindene (**1**) with ozone in CCl_4 at 20 °C gave the expected exo ozonide **29** and the endo isomer **30** in a yield of 72% (the **29**/**30** ratio = 66:34) along with a partially cleavaged product **82** (eq 1). From 1-methyl-2,3-diphenylindene (**5**), a mixture of



1, R = H
5, R = Ph

29, R = H
36, R = Ph

30, R = H
37, R = Ph

82, R = H
83, R = Ph

(1)

the exo/endo ozonide isomers **36** and **37** (the ratio **36**/**37** = 29:71) was obtained in 93% yield together with a small quantity of a partially cleavaged product **83** (eq 1). The structures of the ozonides **30** and **36** have been determined by X-ray analysis.[6] As will be discussed later, it seems initially surprising that the ozonolysis of **5** should give rise to the thermodynamically less stable endo isomer **37** as the major product. We have undertaken, therefore, the ozonolysis of a series of 1-substituted indenes **1–28** and have determined the ratios of the exo/endo isomeric ozonides from each of the respective substrates. We anticipated that careful examination of the steric effects of the substituents in relation to the ozonide stereochemistry could provide further insight into the ozonolysis mechanism.

Table I. Substituent Steric Effects on the Ozonide Exo/Endo Ratio

	substituent			ozonolysis[a,b]		exo/endo ratio in equilibrium[b-d]
indene	R^1	R^2	R^3	exo/endo ratio	% yield	
1	Me	H	Ph	66:34	72[e]	70:30[e]
2	Et	H	Ph	69:31	73	81:19
3	Ph	H	Ph	92:8	74	88:12
4	$(CH_3)_3C$	H	Ph	100:0	71	
5	Me	Ph	Ph	29:71	93[e]	67:33[e]
6	Et	Ph	Ph	23:77	95	93:7
7	$(CH_3)_2CH$	Ph	Ph	20:80	92	97:3
8	Ph	Ph	Ph	78:22	85	75:25
9	$(CH_3)_3C$	Ph	Ph	100:0	85	
10	Me	Ph	H	39:61	47	
11	Et	Ph	H	28:72	66	
12	$(CH_3)_2CH$	Ph	H	3:97	53	
13	Ph	Ph	H	62:38	60	
14	$(CH_3)_3C$	Ph	H	100:0	65	
15	Me	H	Me	67:33	10[e]	
16	Me	Me	Me	68:32	85	
17	Me	Ph	Me	25:75	83[e]	70:30[e]
18	Me	Me	Ph	60:40	83	63:37
19	Me	Et	Ph	39:61	80	67:33
20	Ph	Me	Ph	96:4	71	73:27
21	Ph	Et	Ph	90:10	90	70:30
22	Ph	Me	H	96:4	75	
23	Ph	Et	H	92:8	61	
24	Ph	Ph	Me	85:15	61	

[a] The ozonolysis was performed in CCl_4 at 20 °C. [b] The isolated yield. The ratio was determined by ^{1}H NMR spectroscopy. [c] A methylene chloride solution of an stereoisomeric ozonide and 0.1 equiv of $SbCl_5$ was stirred for an appropriate time. [d] The average value of the exo/endo ratios obtained from two isomers; the deviation of each value from the average value was less than 3%. [e] Taken from the data in ref 6.

Results

(I) Substituent Steric Effects on Ozonide Stereochemistry. The ozonolyses of a series of 1-substituted indenes **1–24** were performed under standard conditions (CCl_4 solution, 20 °C). From the results

---

[1] (a) Osaka University. (b) Heriot-Watt University.

[2] For a recent comprehensive summary of this topic, see: (a) Bailey, P. S. "Ozonation in Organic Chemistry"; Academic Press: New York, 1978, 1982; Vol. 1, Vol. 2. (b) Kuczkowski, R. L. *Acc. Chem. Res.* **1983**, *16*, 42.

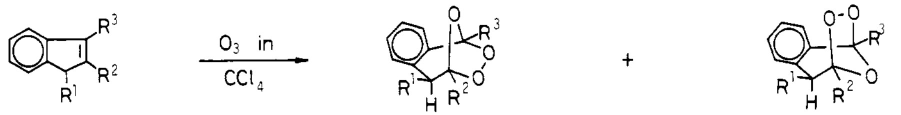
[3] The MO study for ozonolysis: (a) Cremer, D. *J. Am. Chem. Soc.* **1981**, *103*, 3619, 3627. (b) Harding, L. B.; Goddard, W. A. III. *Ibid.* **1978**, *100*, 7180. (c) Hiberty, P. C. *Ibid.* **1976**, *98*, 6088.

[4] The leading references for the ozonolysis in solution: (a) Bailey, P. S.; Ferrell, T. M. *J. Am. Chem. Soc.* **1978**, *100*, 899. (b) Murray, R. W.; Ramachandran, V. *J. Org. Chem.* **1983**, *48*, 813. (c) Murray, R. W.; Su, J.-S. *Ibid.* **1983**, *48*, 817. (d) Bailey, P. S.; Ferrell, T. M.; Rustaiyan, A.; Seyhan, S.; Unruh, L. E. *J. Am. Chem. Soc.* **1978**, *100*, 894. (e) Bauld, N. L.; Thompson, J. A.; Hudson, C. E.; Bailey, P. S. *Ibid.* **1968**, *90*, 1822. (f) Lattimer, P. R.; Kuczkowski, R. L.; Gilles, C. W. *Ibid.* **1974**, *96*, 348. (g) Choe, J.-I.; Kuczkowski, R. L. *Ibid.* **1983**, *105*, 4839. (h) Choe, J.-I.; Srinivasan, M.; Kuczkowski, R. L. *Ibid.* **1983**, *105*, 4703. (i) Reinhardt, H. G.; Doorakian, G. A.; Freedman, H. H. *Ibid.* **1968**, *90*, 5934. (j) Fliszár, S.; Charles, J. *Can. J. Chem.* **1969**, *47*, 3921. (k) Criegee, R.; Batt, S. S.; Von Bornhaupt, B. *Chem. Ber.* **1960**, *23*, 2891.

[5] (a) Miura, M.; Nojima, M. *J. Am. Chem. Soc.* **1980**, *102*, 288. (b) Miura, M.; Nojima, M.; Kusabayashi, S.; Nagase, S. *Ibid.* **1981**, *103*, 1789. (c) Yoshida, M.; Miura, M.; Nojima, M.; Kusabayashi, S. *Ibid.* **1983**, *105*, 6279. (d) Miura, M.; Nojima, M.; Kusabayashi, S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2909. (e) Miura, M.; Ikegami, A.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *Ibid.* **1983**, 1657. (f) Miura, M.; Nagase, S.; Nojima, M.; Kusabayashi, S. *J. Org. Chem.* **1983**, *48*, 2366.

[6] Miura, M.; Ikegami, A.; Nojima, M.; Kusabayashi, S.; McCullough, K. J.; Nagase, S. *J. Am. Chem. Soc.* **1983**, *105*, 2414.

0002-7863/84/1506-2932$01.50/0



(2)

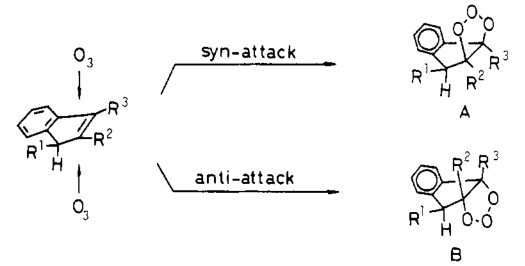
1, R^1 = Me; R^2 = H; R^3 = Ph	29, R^1 = Me; R^2 = H; R^3 = Ph	30, R^1 = Me; R^2 = H; R^3 = Ph
2, R^1 = Et; R^2 = H; R^3 = Ph	31, R^1 = Et; R^2 = H; R^3 = Ph	32, R^1 = Et; R^2 = H; R^3 = Ph
3, R^1 = R^3 = Ph; R^2 = H	33, R^1 = R^3 = Ph; R^2 = H	34, R^1 = R^3 = Ph; R^2 = H
4, R^1 = *t*-Bu; R^2 = H; R^3 = Ph	35, R^1 = *t*-Bu; R^2 = H; R^3 = Ph	
5, R^1 = Me; R^2 = R^3 = Ph	36, R^1 = Me; R^2 = R^3 = Ph	37, R^1 = Me; R^2 = R^3 = Ph
6, R^1 = Et; R^2 = R^3 = Ph	38, R^1 = Et; R^2 = R^3 = Ph	39, R^1 = Et; R^2 = R^3 = Ph
7, R^1 = *i*-Pr; R^2 = R^3 = Ph	40, R^1 = *i*-Pr; R^2 = R^3 = Ph	41, R^1 = *i*-Pr; R^2 = R^3 = Ph
8, R^1 = R^2 = R^3 = Ph	42, R^1 = R^2 = R^3 = Ph	43, R^1 = R^2 = R^3 = Ph
9, R^1 = *t*-Bu; R^2 = R^3 = Ph	44, R^1 = *t*-Bu; R^2 = R^3 = Ph	
10, R^1 = Me; R^2 = Ph; R^3 = H	45, R^1 = Me; R^2 = Ph; R^3 = H	46, R^1 = Me; R^2 = Ph; R^3 = H
11, R^1 = Et; R^2 = Ph; R^3 = H	47, R^1 = Et; R^2 = Ph; R^3 = H	48, R^1 = Et; R^2 = Ph; R^3 = H
12, R^1 = *i*-Pr; R^2 = Ph; R^3 = H	49, R^1 = *i*-Pr; R^2 = Ph; R^3 = H	50, R^1 = *i*-Pr; R^2 = Ph; R^3 = H
13, R^1 = R^2 = Ph; R^3 = H	51, R^1 = R^2 = Ph; R^3 = H	52, R^1 = R^2 = Ph; R^3 = H
14, R^1 = *t*-Bu; R^2 = Ph; R^3 = H	53, R^1 = *t*-Bu; R^2 = Ph; R^3 = H	
15, R^1 = R^3 = Me; R^2 = H	54, R^1 = R^3 = Me; R^2 = H	55, R^1 = R^3 = Me; R^2 = H
16, R^1 = R^2 = R^3 = Me	56, R^1 = R^2 = R^3 = Me	57, R^1 = R^2 = R^3 = Me
17, R^1 = R^3 = Me; R^2 = Ph	58, R^1 = R^3 = Me; R^2 = Ph	59, R^1 = R^3 = Me; R^2 = Ph
18, R^1 = R^2 = Me; R^3 = Ph	60, R^1 = R^2 = Me; R^3 = Ph	61, R^1 = R^2 = Me; R^3 = Ph
19, R^1 = Me; R^2 = Et; R^3 = Ph	62, R^1 = Me; R^2 = Et; R^3 = Ph	63, R^1 = Me; R^2 = Et; R^3 = Ph
20, R^1 = R^3 = Ph; R^2 = Me	64, R^1 = R^3 = Ph; R^2 = Me	65, R^1 = R^3 = Ph; R^2 = Me
21, R^1 = R^3 = Ph; R^2 = Et	66, R^1 = R^3 = Ph; R^2 = Et	67, R^1 = R^3 = Ph; R^2 = Et
22, R^1 = Ph; R^2 = Me; R^3 = H	68, R^1 = Ph; R^2 = Me; R^3 = H	69, R^1 = Ph; R^2 = Me; R^3 = H
23, R^1 = Ph; R^2 = Et; R^3 = H	70, R^1 = Ph; R^2 = Et; R^3 = H	71, R^1 = Ph; R^2 = Et; R^3 = H
24, R^1 = R^2 = Ph; R^3 = Me	72, R^1 = R^2 = Ph; R^3 = Me	73, R^1 = R^2 = Ph; R^3 = Me

Table II. Ozonolysis of 1-Methyl-2,3-diarylindenes–The Substituent Electronic Effects on the Ozonide Exo/Endo Ratio[a]

	substituent		ozonide[b]	
indene	X	Y	exo/endo ratio	% yield
25	OMe	H	23:77	89
26	H	OMe	23:77	85
5	H	H	29:71	93
27	Cl	H	45:55	91
28	H	Cl	37:93	95

[a, b] See the footnotes in Table I.

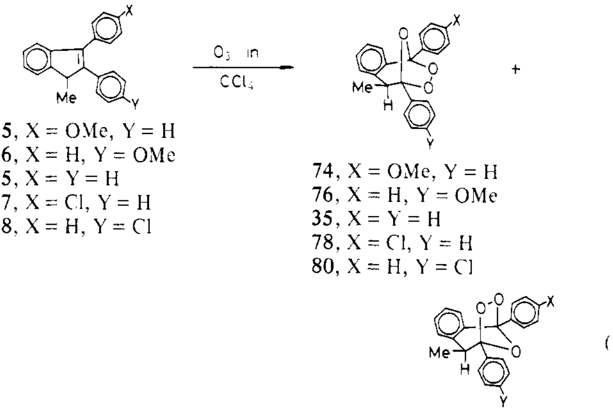
Scheme I



(Table I), it is clear that the ozonide isomer ratios vary markedly with the nature of the 1-substituent in the indene substrates. The ozonolysis of 1-substituted 3-phenylindenes **1–4** gave predominantly the corresponding exo ozonides, the exo/endo ratio increasing with the steric bulk of the 1-substituent. In the most extreme case, 1-*tert*-butyl-3-phenylindene (**4**) afforded only the exo isomer **35** in high yield. Conversely ozonolyses of 1-methyl-, 1-ethyl-, and 1-isopropyl-2,3-diphenylindenes (**5–7**) yielded predominantly the thermodynamically less stable endo ozonides, the exo/endo ratios being 29:71, 23:77, and 20:80, respectively. A similar trend was also observed for 1-methyl-, 1-ethyl-, and 1-isopropyl-2-phenylindenes (**10–12**). These latter results indicate that the ozonide exo/endo ratio decreases inversely to the steric bulk of the 1-substituent. The ozonolyses of more bulky 1-phenyl- and 1-*tert*-butyl-2,3-diphenylindenes (**8** and **9**), however, afforded predominantly or exclusively the corresponding exo ozonides as did the 1-phenyl- and 1-*tert*-butyl-2-phenylindenes (**13** and **14**).

The steric bulk of the 2-substituent of the indenes also seems to play an important role in determining the ozonide exo/endo ratio. In the series of 2-substituted 1-methyl-3-phenylindenes **1**, **5**, **18**, and **19**, the ozonide exo/endo ratios decreased in the order H (66:34) > Me (60:40) > Et (39:61) > Ph (29:71). These results demonstrate that the exo/endo ratio decreases with the increase in steric bulk of the 2-substituent. Similar trends were also observed from the ozonolyses of the 2-substituted 1,3-dimethylindenes **15–17**. For the 2-substituted 1,3-diphenylindenes **3**, **8**, **20**, and **21**, however, the exo/endo ratio decreased in the order Me (96:4) > H (92:8) > Et (90:10) > Ph (78:22).

(II) Substituent Electronic Effects on the Ozonide Stereochemistry. To investigate the influence of substituent electronic effects on ozonide stereochemistry, the ozonolyses of 1-methyl-2,3-diarylindenes **5** and **25–28** were undertaken (eq 3). The data in Table II suggest that the substituent electronic effects have a small but significant influence on the ozonide exo/endo ratio. The ozonolysis of 1-methyl-2-phenyl-3-(4-anisyl)indene (**25**) and 1-methyl-2-(4-anisyl)-3-phenylindene (**26**) gave a mixture of the exo/endo ozonide isomers **74**/**75** and **76**/**77**. The ratio, 23:77 in each case, deviates only slightly from the exo/endo ratio 29:71 obtained from the ozonolysis of 1-methyl-2,3-diphenylindene (**5**). In direct contrast, the **78**/**79** ratio 45:55 from 1-methyl-2-phenyl-3-(4-chlorophenyl)indene (**27**) and the **80**/**81** ratio 36:64 from 1-methyl-2-(4-chlorophenyl)-3-phenylindene (**28**) were substantially larger than the ratio of 29:71 from **5**. In other words, the ozonide exo/endo ratio increased as the electron-withdrawing



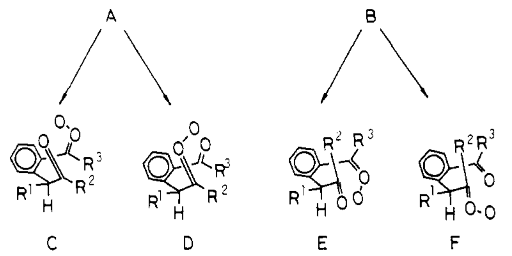
25, X = OMe, Y = H
26, X = H, Y = OMe
5, X = Y = H
27, X = Cl, Y = H
28, X = H, Y = Cl

74, X = OMe, Y = H
76, X = H, Y = OMe
35, X = Y = H
78, X = Cl, Y = H
80, X = H, Y = Cl

(3)

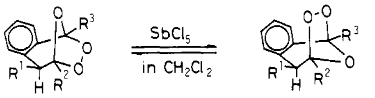
75, X = OMe, Y = H
77, X = H, Y = OMe
36, X = Y = H
79, X = Cl, Y = H
81, X = H, Y = Cl

Scheme II



ability of the substituents X or Y decreased.

(III) Relative Thermodynamic Stabilities between an Exo Ozonide and the Endo Isomer. It has been shown that the exo/endo ozonides can be equilibrated in the presence of suitable acids (eq 4 and Table I):[6,7] When *exo*-1-methyl-3-phenylindene ozonide



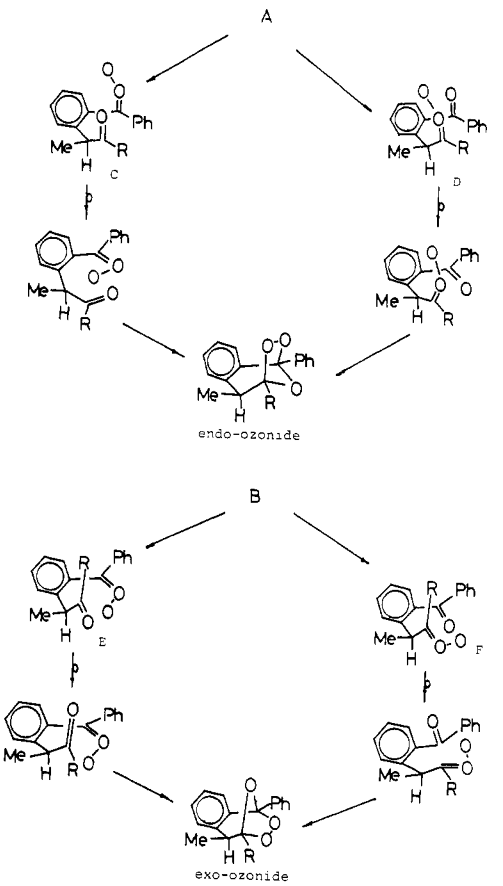
(4)

(**29**) was treated with 0.1 mol equiv of $SbCl_5$ in CH_2Cl_2 for 2 h, a mixture of **29** and the endo isomer **30** was recovered in a yield of 21%, the exo/endo ratio being 71:29. The reaction of **30** under similar conditions resulted in a recovery of 28% yield of a mixture of 69% **29** and 31% **30**. These results indicated that exo ozonide **29** is more stable than the endo isomer **30**. Consistent with this, the exo/endo ratios were found to be around 7:3 for all the pairs of 1-methylindene ozonides. The acid-catalyzed interconversion of the 1-substituted 3-phenylindene ozonide pairs **29**/**30**, **31**/**32**, and **33**/**34** revealed that the exo/endo equilibrium ratios increased directly with the steric bulk of the 1-substituent. For the 1-substituted 2,3-diphenylindene ozonide pairs **36**/**37**, **38**/**39**, **40**/**41**, and **42**/**43**, the exo/endo ratios in equilibrium increased in the order Me (67:33) < Ph (75:25) < Et (93:7) < isopropyl (97:3). Not unexpectedly, under the acidic conditions, the *exo*-1-*tert*-butylindene ozonides **35** and **44** did not rearrange to the corresponding endo isomers. Overall these results demonstrate that the exo ozonide is generally the thermodynamically more stable isomer and the steric effects of the 1-substituent exert a significant though somewhat complicated effect on the relative thermodynamic stabilities of the exo/endo ozonide isomers. Moreover, the exo/endo ratios **36**/**37**, **38**/**39**, and **40**/**41** at equilibrium were noted to be significantly different from those obtained directly from the ozonolysis of **5** (29:71), **6** (23:77), and **7** (20:80).

Discussion

In general no mechanism other than the Criegee three-step mechanism has been demonstrated to be of major importance in liquid-phase ozonolysis.[2] Although some of our results do suggest that the overall reaction may not proceed under thermodynamic control,[8] there is no overwhelming experimental evidence to question the applicability of this mechanism to the ozonolysis of indenes (as distinct from other olefins).[9] Consequently we have

Scheme III



attempted to rationalize our results within the framework of this model.

The initial step in the reaction of ozone with a 1-substituted indene would be the formation of the primary ozonide(s). Although the work of Reinhardt et al.[4i] on the ozonolysis of substituted cyclobutenes favors approach of ozone exclusively from the less hindered face, the five-membered ring of the indene system is probably less sterically congested and more open to approach from either face, in most cases, to give both primary ozonides A and B (Scheme I).[10,11] Assuming the normal sequence of events, scission of the primary ozonides A and B would give rise to the carbonyl/carbonyl oxide pairs C/D and E/F, respectively (Scheme II), which on intramolecular recombination would yield the final exo/endo ozonides.[9,12]

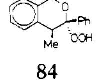
From the mechanism, it is possible that the substrate substituents could influence the reaction pathway at any of the key steps: the initial addition of ozone to form primary ozonides A and B, the subsequent cleavage direction of these adducts, and also the recombination of the carbonyl/carbonyl oxide fragments.

---

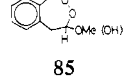
[7] A referee has pointed out that low recoveries of the ozonide pair **29**/**30** raise some questions about the true relative thermodynamic stabilities. When the interconversion was performed in the presence of $ClSO_3H$ in CH_2Cl_2 or in AcOH, however, a mixture of the ozonides **29** and **30** was recovered in around 60% yield (the equilibrium ratio **29**/**30** = 70:30).[6] Moreover, treatment of either **60** or **61** with $SbCl_5$ in CH_2Cl_2 lead to the recovery of more than 60% yield of the ozonide pair **60**/**61** (Experimental Section). These results would suggest that the observed exo/endo ratios correspond to the relative thermodynamic stabilities.

[8] MO calculations for the ozonolysis of simple alkenes have revealed that the third step (formation of final ozonides) is highly exothermic; according to Hammond postulate, then the structure of the transition state in this step would be similar to the reactant rather than the product.[3a] The predominant formation of the less stable endo ozonides would be consistent with this hypothesis.

[9] Ozonolysis of **5** in methanol at −70 °C afforded, in addition to the expected ozonides **36** and **37** (27%), a solvent-participated product as a single isomer in moderate yield (46%). The crystal structure, as determined by X-ray analysis, is depicted in formula **84**. Although this structure differs markedly



84



85

from that of the solvent-participated ozonolysis product from indene **85**, it is consistent, however, with the intermediacy of the Criegee-type carbonyl/carbonyl oxide pairs such as C–F: McCullough, K. J.; Nojima, M.; Miura, M.; Fujisaka, T.; Kusabayashi, S. *J. Chem. Soc., Chem. Commun.* **1984**, 35.

[10] The formation of the partial cleavaged products **82**/**83** demonstrates that a process via a peroxy epoxide or the equivalents may participate competitively, but to a small extent.[11]

[11] Bailey, P. S.; Lane, A. G. *J. Am. Chem. Soc.* **1967**, *89*, 4473.

[12] Sawaki, Y.; Kato, H.; Ogata, Y. *J. Am. Chem. Soc.* **1981**, *103*, 3833.

It has been shown that in the ozonolysis of styrene derivatives, the direction of cleavage of the primary adduct is sensitive to the nature of the aromatic ring substituent.[13] In general, electron-donating substituents in the aryl group stabilize the carbonyl oxide moiety. Assuming analogous substituent effects, the ozonide isomer ratios have been determined (Table II) for a series of 1-methyl-2,3-diarylindenes **5** and **25**–**28** to examine the importance of the direction of cleavage of the primary ozonides. On the basis of previous results,[13] the ratio of the carbonyl/carbonyl oxide pairs C/D and E/F obtained on ozonolysis of **25** (X = OMe) and **28** (Y = Cl) would be expected to be significantly greater than those from **26** (Y = OMe) and **27** (X = Cl), with the ratio from **5** (X = Y = H) having some intermediate value. If the final ozonide stereochemistry depends appreciably on the direction of cleavage of adducts A and B, then the deviations of the ozonide exo/endo ratios **74**/**75** and **80**/**81** from the ratio **36**/**37** should at least be the same in sense, though not necessarily in magnitude. Furthermore, the ratios **76**/**77** and **78**/**79** should deviate from the ratio **36**/**37** in the opposite sense.

In reality, the experimental results do not satisfy the above expectations. The exo/endo isomer ratio appears to vary directly with the electron-withdrawing ability of the substituent, irrespective of the phenyl group in which it is located. Because of the lack of information regarding substituent electronic effects on the direction of cleavage of the primary ozonides A and B,[14] however, we can only say that this inconsistency between the predicted and experimental results offers little support for the hypothesis that the direction of cleavage of primary ozonide is a major factor in determining the ozonide stereochemistry.

Since factors such as relative thermodynamic stabilities of the isomeric pairs and the cleavage direction of the primary ozonides offer little assistance in rationalizing our results, the direction of approach of ozone with respect to the substrate is now considered. Unlike the previous two, this aspect is not so amenable to direct experimental investigation since the primary adducts are not stable under usual conditions. On scission of the primary ozonide A or B, it seems likely that the resulting carbonyl and carbonyl oxide groups would be formed on the same side of the molecular plane. However, before recombination of this pair to produce the 1,2,4-trioxolane ring, one of the moieties must reorientate by some 180° (Scheme III). In these sterically congested systems, the carbonyl group probably would be more free to rotate as required than the adjacent carbonyl oxide moiety. If the subsequent re-addition of the group is comparatively fast, then it would be expected that the syn adduct A should lead to the selective formation of the endo ozonide. Conversely, the exo ozonide would be derived predominantly from the anti isomer B.

Assuming the aforementioned mechanism, the ratio of exo/endo bicyclic ozonides derived from the 1-substituted 3-phenylindenes **1**–**4** should increase as a function of the steric bulk of the 1-substituent,[15,16] since the syn-mode attack by ozone would be increasingly retarded. The product distributions from this series exhibit trends consistent with the above hypothesis (Table I, entries 1–4). The proportion of the exo isomer increases steadily with the bulk of the 1-substituent until, when it is a *tert*-butyl group as in **4**, only the exo isomer was obtained. Steric overcrowding in **4** almost certainly directs the ozone to the anti face producing the corresponding adduct of type B from which ozonide **35** is derived.

The ozonolysis results from the 1-substituted 2,3-diphenylindenes **5**–**9** are less consistent than above. On one hand, the 1-methyl, 1-ethyl, and 1-isopropyl derivatives **5**–**7** each give the thermodynamically less stable endo stereoisomers as the major product whereas the 1-phenyl and 1-*tert*-butyl compounds **8** and **9** afford mainly the expected exo isomer in each case. The isomer distributions from compounds **8** and **9** are clearly in accord with those from indenes **3** and **4**, respectively, and indicative of a similar preponderance of anti attack by ozone on these substrates. Because of the marked differences in product ratios within the trisubstituted series, and also in comparison with the disubstituted indenes **1** and **2**, it seems reasonable to consider that an alternative mechanism was in operation for indenes **5**–**7**. In this instance, the merits of a predominantly syn mode of addition should be explored, particularly in relation to the conformational preferences of the substrates.[17]

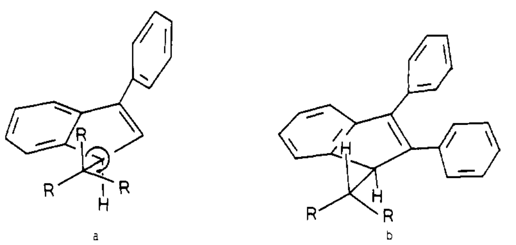


Figure 1.

In the 1-methyl- and 1-ethyl-3-phenylindenes **1** and **2**, the alkyl groups at C-1 should be comparatively free to rotate (Figure 1a) whereas in systems **5**–**7**, the 2-phenyl substituent would preclude free rotation of the corresponding 1-alkyl groups, the alkyl groups would adopt staggered conformations in which an α-hydrogen would be uppermost as depicted in Figure 1b. Such conformations would not only reduce the relative steric hindrance to a syn approach by ozone but may also account for the similarity in the product ratios obtained from **5**–**7**.

The steric interactions that arise from the contiguous substitution pattern in indenes **5**–**7** could distort the five-membered ring sufficiently to force the 1-alkyl substituent into a more conventional equatorial position, thereby rendering the syn face more susceptible to attack. In addition, the adjacent hydrogen atom at C-1 would offer increased hindrance to the alternative anti approach as a consequence of any distortion.

Finally, there is some experimental evidence that 2-phenyl substitution disfavors to some extent the anti approach of ozone. Ozonolysis of 1,2-diphenylindene (**13**) and 2-methyl-1-phenylindene (**22**) affords exo/endo ratios of 62:38 and 95:5, respectively. Since the steric interactions for a syn approach would be similar in each case, it seems likely that a 2-phenyl group offers a greater retarding effect to anti approach than a 2-methyl group, arising perhaps from greater eclipsing interactions in the transition state for formation of isomer B. In the trisubstituted indenes **5**–**7**, the 2-phenyl substituent, being essentially perpendicular to the indene plane,[17] would exert an even greater effect on the approach of ozone from the anti face than in **13**.

Therefore, in the absence of additional experimental evidence, it is tentatively proposed that, as a consequence of the concerted application of the above factors the reaction of ozone with indenes **5**–**7** proceeds predominantly by a syn mode of addition to give primary ozonides of type A, which in turn yield the corresponding endo ozonides. Owing to the similarity in product distribution from the 1-alkyl-2-phenylindenes **10**–**12**, it is likely that related mechanisms are also operative for these systems. As a corollary, if the ozone tends to approach the indene substrates from the anti face as postulated for the cyclobutenes,[4i] then the lack of consistency in the experimental results would imply that the details of the mechanism that determine product stereochemistry are

---

(13) Fliszár, S.; Granger, M. J. *J. Am. Chem. Soc.* **1969**, *91*, 3330.

(14) For example, the ozonolysis of **5** in methanol afforded, together with a solvent-participated product **84**,[9] considerable amounts of ozonides **36** and **37**. Therefore, the method used in determining the direction of cleavage of styrene derivatives[13] cannot be used in the case of the 1-substituted indenes.

(15) Diborane attacks the double bond of 1-substituted 3-phenylindenes **1**–**3** from both faces, the ratio of anti/syn attack being increased in the order Me (75:25) < Et (88:12) < Ph (100:0).[16]

(16) Miura, M.; Yoshida, M.; Nojima, M.; Kusabayashi, S. *J. Chem. Soc., Perkin Trans. 1* **1982**, 97.

(17) From models, the indene moiety is essentially planar with the 1-alkyl group in a pseudoequatorial position and the planes of the phenyl groups roughly perpendicular to the indene plane. In the 1,3-disubstituted indenes with only a hydrogen at C-2 it seems likely that the alkyl group at C-1 should be free to rotate about the σ-single bond. On the other hand, in the 1,2,3-trisubstituted indenes, free rotation of the alkyl group at C-1 would be precluded by the presence of the adjacent phenyl group at C-2 (Figure 1). It is likely that this group at C-1 would adopt close to a minimum energy conformation, and the molecule would be essentially conformationally rigid owing to "buttressing" steric interactions between the adjacent groups.

somewhat obscure.[18] Moreover, it is difficult to invoke solvent and/or temperature effects.[19]

Experimental Section

General Procedure. ^{1}H NMR spectra were obtained with a JMN-PS-100 spectrometer in $CDCl_3$. MS data were obtained with a Hitachi RMU-6H spectrometer and infrared spectra with a Hitachi 215 spectrometer. Ozonolyses were carried out with the use of 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. All melting points are not corrected.

Preparation of Indenes. 1,3-Diphenylindene (**3**),[20] 1-methyl-2,3-diphenylindene (**5**),[21] 1,2,3-triphenylindene (**8**),[22] 1,3-dimethylindene (**15**),[23] 1,2,3-trimethylindene (**16**),[24] and 1,2-diphenyl-3-methylindene (**24**)[21] were prepared according to the reported methods. 1-Methyl-, 1-ethyl-, 1-*tert*-butyl-, 1,2-dimethyl-, and 1-methyl-2-ethyl-3-phenylindenes, **1**, **2**, **4**, **18**, and **19**, were obtained by the reactions of phenylmagnesium bromide with 3-methyl-1-indanone,[25] 3-ethyl-1-indanone,[26] 3-*tert*-butyl-1-indanone,[27] 2,3-dimethyl-1-indanone,[24] and 2-ethyl-3-methyl-1-indanone (prepared from acetophenone and ethyl 2-bromobutylate by the method of Plattner et al.[24]) followed by heating at 160 °C under reduced pressure (20 mmHg) and subsequent purification by column chromatography on silica gel using petroleum ether as eluant. The indene **1** was a solid, mp 32–34 °C (from methanol, lit.[28] 36–37 °C). **2** was an oil: NMR δ 0.98 (t, *J* = 7.5 Hz, 3 H), 1.40–2.20 (m, 2 H), 3.52 (t × d, *J* = 7.5, 2.6 Hz, 1 H), 6.56 (d, *J* = 2.6 Hz, 1 H). **4** was an oil: NMR δ 1.08 (s, 9 H), 3.33 (d, *J* = 7.5 Hz, 1 H), 6.48 (d, *J* = 2.6 Hz, 1 H). **18** was an oil: NMR δ 1.33 (d, *J* = 7.5 Hz, 3 H), 2.00 (s, 3 H), 3.23 (q, *J* = 7.5 Hz, 1 H). **19** was an oil: NMR δ 1.10 (t, *J* = 7.5 Hz, 3 H), 1.33 (d, *J* = 7.5 Hz, 3 H), 1.98–2.84 (m, 2 H), 3.43 (q, *J* = 7.5 Hz, 1 H). 1-Substituted 2-phenylindenes **11–15** were prepared by reduction of 3-methyl,[21] 3-ethyl, 3-isopropyl, 3-phenyl,[22] and 3-*tert*-butyl-2-phenylindanones, which were obtained from the corresponding 3-substituted 2,3-diphenylpropionic acids,[21,29] with lithium aluminum hydride or sodium borohydride, followed by dehydration with anhydrous oxalic acid at 120 °C and subsequent purification by column chromatography on silica gel using petroleum ether as eluant. The indene **11** was a solid: mp 53–54 °C (from methanol); NMR δ 1.2 (d, *J* = 7.5 Hz, 3 H), 3.80 (q, *J* = 7.5 Hz, 1 H), 6.98 (s, 1 H). **12** was obtained as an oil containing 2-phenyl-3-ethylindene (15%): NMR δ 1.46 (d, *J* = 7.5 Hz, 3 H), 1.96 (q × d, *J* = 7.5, 6.0 Hz, 2 H), 3.86 (t, *J* = 6.0 Hz, 1 H), 6.94 (s, 1 H). **13** was an oil: NMR δ 0.34 (d, *J* = 7.5 Hz, 3 H), 1.26 (d, *J* = 7.5 Hz, 3 H), 2.02–2.66 (m, 1 H), 3.90 (d, *J* = 3.0 Hz, 1 H), 6.94 (s, 1 H). **14** was a solid, mp 176–178 °C (from methanol–benzene, lit.[30] 177–178 °C). **15** was a solid: mp 63–64 °C (from petroleum ether); NMR δ 0.84 (s, 9 H), 3.40 (s, 1 H), 6.72 (s, 1 H). The reaction of 2-methyl- or 2-ethyl-3-phenylindanones, which were prepared by reduction of 2-methyl-[31] or 2-ethyl-3-phenylindenones[32] with zinc powder in acetic acid,[22] with phenylmagnesium bromide or with lithium aluminum hydride and subsequent dehydration, as described above, afforded the corresponding 1-phenylindenes **20–23**. The indene **20** was a solid: mp 96–97 °C (from methanol); NMR δ 1.86 (s, 3 H), 4.40 (s, 1 H). **21** was an oil: NMR δ 1.02 (t, *J* = 7.5 Hz, 3 H), 1.66–2.52 (m, 2 H), 4.46 (s, 1 H). **22** was a solid containing 10% 2-methyl-3-phenylindene: mp 40–43 °C (from petroleum ether); NMR δ 2.10 (s, 3 H), 4.26 (s, 1 H), 6.56 (br s, 1 H). **23** was an oil containing 14% 2-ethyl-3-phenylindene: NMR δ 1.10 (t, *J* = 7.5 Hz, 3 H), 2.24 (q, *J* = 7.5 Hz, 2 H), 4.30 (s, 1 H), 6.50 (br s, 1 H). 3-Methyl-, 3-(4-methoxyphenyl)-, and 3-(4-chlorophenyl)-1-methyl-2-phenylindenes (**17**, **25**, and **27**) were prepared by the reactions of 2-phenyl-3-methylindanone[21] with methyl-, 4-methoxyphenyl-, and 4-chlorophenylmagnesium reagents. The indene **17** was a solid, mp 72–74 °C (from ethanol, lit.[33] 73–74 °C). **25** was a solid, mp 119–120 °C (from methanol). **27** was a solid, mp 134–135 °C (from ethanol). 1-Ethyl-, 1-isopropyl-, and 1-*tert*-butyl-2,3-diphenylindenes (**6**, **7**, and **9**) were prepared by the method of Huffman and Ullman;[34] the reactions of 2,3-diphenylindenone with ethyl-, isopropyl-, and *tert*-butylmagnesium reagents followed by treatment with 57% HI in refluxing acetic acid afforded the corresponding indenes **6**, **7**, and **9**. **6** was a solid: mp 71–72 °C (from methanol); NMR δ 0.53 (t, *J* = 7.5 Hz, 3 H), 1.86 (q × d, *J* = 7.5, 6.0 Hz, 2 H), 4.06 (t, *J* = 6.0 Hz, 1 H). **7** was a solid: mp 139–141 °C (from methanol); NMR δ 0.40 (d, *J* = 7.5 Hz, 3 H), 1.24 (d, *J* = 7.5 Hz, 3 H), 1.73–2.46 (m, 1 H), 4.00 (d, *J* = 4.0 Hz, 1 H). **9** was a solid: mp 88–90 °C (from methanol); NMR δ 0.86 (s, 9 H), 3.86 (s, 1 H). The reaction of 2-(4-chlorophenyl)-3-phenylindenone with methylmagnesium iodide gave 1-methyl-2-(4-chlorophenyl)-3-phenylindene (**28**) as a solid: mp 155–157 °C (from ethanol–benzene); NMR δ 1.28 (d, *J* = 7.5 Hz, 3 H), 4.02 (q, *J* = 7.5 Hz, 1 H). 1-Methyl-2-(4-methoxyphenyl)-3-phenylindene (**26**) was prepared by the reaction of 2-(4-methoxy)-3-methyl-1-indanone, obtained from the reaction of 4-methoxy-phenylacetic acid with acetophenone,[35] with phenylmagnesium bromide and subsequent dehydration by application of heat: mp 103–104 °C (from petroleum ether); NMR δ 1.26 (d, *J* = 7.5 Hz, 3 H), 3.64 (s, 3 H), 3.86 (q, *J* = 7.5 Hz, 1 H).

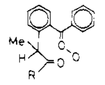
Ozonolysis Procedure. The procedure has been described previously.[6] Configurations of ozonide exo/endo pairs were determined as described before.[6] The physical properties of ozonides **29–81** are listed in Table III (supplementary material). The exo/endo ratios were determined by comparison of the peak areas of C-1 hydrogens of exo/endo isomers in NMR spectra.

Acid-Catalyzed Interconversion of an Exo/Endo Ozonide Pair.[6] To a solution of *exo*-1,2-dimethyl-3-phenylindene ozonide (**60**) (270 mg, 2 mmol) in CH_2Cl_2 (10 mL) was added a mixture of $SbCl_5$ (60 mg, 0.2 mmol) and CH_2Cl_2 (2 mL) in one portion, and the mixture was stirred at 20 °C for 2 h. By column chromatography on silica gel using benzene–petroleum ether (1:1) as eluant, a mixture of **60** and **61** was recovered in a yield of 68%. The **60**/**61** ratio was determined to be 66:34 by the NMR spectroscopy. From the reaction of the endo ozonide **61** under identical conditions was obtained 63% yield of a mixture of 62% **60** and 38% **61**.

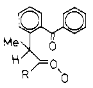
Supplementary Material Available: A list of the physical properties of the ozonides **29–81** (Table III) (6 pages). Ordering information is given on any current masthead page.

---

(18) It should be noted that our discussion does not involve syn/anti carbonyl oxide concepts. Molecular models suggest that anti forms G and H would not have correct geometry for a so-called 1,3-dipolar intramolecular cycloaddition. Polymeric products in the ozonolysis of **1** may be derived from the corresponding anti carbonyl oxides G and H.[6] In the ozonolysis of **5**, however, ozonides **36** and **37** were obtained almost quantitatively. It does not seem realistic that the reaction proceeds only via the syn carbonyl oxides C–F. Thus, these results may demonstrate that a nonconcerted process to give final ozonides participates to some extent,[4b,c] or, alternatively, anti carbonyl oxides G and H convert into the syn intermediates C–F by a process involving intramolecular interactions with the carbonyl moiety.[4a]



G



H

(19) From some preliminary work on 1-methyl-2,3-diphenylindene (**5**) it has been shown that temperature and solvent determine not only the isomer distributions, but also the products observed. For example, ozonolysis of **5** in CCl_4/MeOH (1:1) at 20 °C gives the normal ozonides **36** and **37** in high yield (71%) but with an exo/endo ratio 46:54. Ozonolysis of **5** in CH_2Cl_2/MeOH (3:2) at −70 °C gave ozonides **36** and **37** in substantially reduced quantity (27%, isomer ratio 59:41) together with the solvent-participated product **84**[9] in 46% yield.

(20) Koelsch, C. F.; Johnson, P. R. *J. Org. Chem.* **1941**, *6*, 534.

(21) Koelsch, C. F.; Johnson, P. R. *J. Am. Chem. Soc.* **1943**, *65*, 567.

(22) Koelsch, C. F. *J. Am. Chem. Soc.* **1934**, *56*, 1337.

(23) Meuring, L. *Acta Chem. Scand., Ser. B* **1974**, *B28*, 295.

(24) Plattner, P. A.; Furstand, A.; Jirasek, K. *Helv. Chim. Acta.* **1947**, *30*, 1320.

(25) Koelsch, C. F.; Hochmann, H.; Le Claire, C. D. *J. Am. Chem. Soc.* **1943**, *65*, 59.

(26) Sorlin, G.; Bergson, G. *Ark. Kemi* **1968**, *29*, 593.

(27) Koelsch, C. F. *J. Am. Chem. Soc.* **1943**, *65*, 1640.

(28) Bertali, V.; Plesch, P. H. *J. Chem. Soc. B* **1968**, 1500.

(29) Auerbach, R. A.; Kingsbury, C. A. *Tetrahedron* **1971**, *27*, 2069.

(30) Orechoff, A. *Ber.* **1914**, *47*, 89.

(31) De Fagi, R. *Gazz. Chim. Ital.* **1915**, *45*, II, 143.

(32) Frank, R. L.; Eklund, H.; Richter, J. W.; Vanneman, C. R.; Wennerberg, A. N. *J. Am. Chem. Soc.* **1944**, *66*, 1.

(33) Fiato, R. A.; Mustak, P.; Battiste, A. *J. Chem. Soc. Chem. Commun.* **1975**, 869.

(34) Huffman, K. R.; Ullman, E. F. *J. Am. Chem. Soc.* **1967**, *89*, 5629.

(35) Zimmerman, H. E.; Aasen, S. M. *J. Org. Chem.* **1978**, *43*, 1493.