Ozonolyses of 1,2-Diphenyl- and 2-Phenylindene

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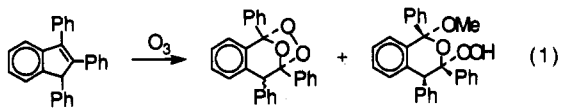
Ozonolyses of 1,2-diphenylindene (**7**), 2-phenylindene (**18**), and the structurally related acyclic keto olefins **13**, **14**, **26**, and **32** were conducted in $MeOH/CH_2Cl_2$ at −70 and 0 °C. The structure of the indenes, **7** and **18**, and the reaction temperature, were found to exert an influence on the outcome of the reaction. Ozonolysis of 1,2-diphenylindene (**7**) at −70 °C proceeded exclusively via the carbonyl oxide intermediate **15** providing the methanol-derived isochroman **9a** as the sole isolable product. In contrast, four methanol-derived products, **20**–**23**, were obtained from 2-phenylindene (**18**) under similar reaction conditions, suggesting that the primary ozonide **25** from **18** undergoes two competing modes of decomposition. Ozonolyses of indenes, **7** and **18**, and 0 °C gave mainly the corresponding ozonides, **8** and **19**, respectively, while analogous reactions at −70 °C resulted in the predominant formation of the methanol-derived products **9** and **20**–**23**, respectively. The major differences in composition between the ozonolysis product mixtures derived from the acyclic keto olefins **13**, **14**, **26**, and **32** and the appropriate corresponding indenes **7** and **18** suggest that the intermediate carbonyl oxides generated from the former do not make significant contributions to the reaction pathways of the latter.

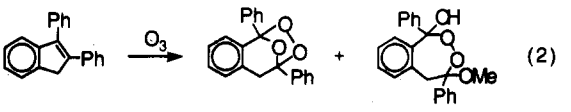
During our continuing studies on the mechanism of ozonolysis of indene derivatives[2] we have discovered that the ozonolysis of 1,2,3-triphenylindene (**1**) in aprotic solvents yields the corresponding ozonide **2** (mainly the exoisomer) almost quantitatively, whereas the reaction in methanol results in the exclusive formation of a novel isochroman derivatives **3** (eq 1).[2a] In marked contrast,



(1)

1 2 3

ozonization of 2,3-diphenylindene (**4**) yielded predominantly ozonide **5** irrespective of the solvent except in methanol–methylene chloride at −70 °C when a more conventional hemiperacetal **6** was also obtained, albeit in a low yield (14% yield) (eq 2).[2b] To investigate further



(2)

4 5 6

the influence of a phenyl substituent at C-1, we have conducted ozonolyses of 1,2-diphenylindene (**7**) and 2-phenylindene (**18**).

Results and Discussion

Ozonolysis of 1,2-Diphenylindene (7). Treatment of a solution of indene **7** in $MeOH/CH_2Cl_2$ with ozone (1.5 equiv) at −70 °C gave a crystalline methoxy hydroperoxide (51% yield) as the sole isolable product; starting material was also recovered (40% yield) (Scheme I and Table I). Since the structure of this product was ambiguous, an X-ray crystallographic analysis of suitable crystals of this solvent-derived product was undertaken.

The results of the X-ray analysis are illustrated in Figure 1, together with the numbering system adopted in this study.[3] A cursory inspection of Figure 1 indicates that the solvent-derived product from **7** is the isochroman derivative **9a**, in which the vicinal hydroperoxy and phenyl groups on C(1) and C(2) respectively are trans related. This geometrical arrangement suggests that **9a** has been produced by a reaction pathway analogous to that of **3** obtained from indene **1**. Consistent with its molecular structure, treatment of **9a** with trifluoroacetic acid in methylene chloride results in the exclusive formation of *exo*-1,2-diphenylindene ozonide (*exo*-**8**).

Reaction of **7** in the same solvent system at 0 °C gave mainly ozonide **8** (40% yield of *exo*-**8** and 11% yield of *endo*-**8**; for the assignment of the stereochemistry of **8**, see the discussion in 2) and **9a** (29% yield). In addition, however, an isomeric isochroman derivative **9b** (in the ^1H NMR spectra the characteristic signal attributable to the hydroperoxy proton appears at δ 9.30[2]) was also obtained in small quantities (4% yield) (Table I). The cis relationship between the vicinal phenyl and hydroperoxy groups was confirmed by the fact that treatment of this isochroman derivative with trifluoroacetic acid in CH_2Cl_2 led to the formation of the ozonide *endo*-**8** (the configuration of the methoxy group in **9b** was, however, not determined).

A summary of the mechanism of ozonolysis of 1,2-diphenylindene (**7**) is outlined in Scheme I. Following the initial attack of ozone to indene **7**, it was expected that the resulting primary ozonide (PO) **12** should, a priori, undergo cleavage by either of the two possible modes (paths a and b) providing the carbonyl oxide intermediates **15** and **16**, respectively. Ozonolysis of keto olefin **13**, from

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

(2) (a) Nakamura, N.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 1799. (b) McCullough, K. J.; Nakamura, N.; Fujisaka, T.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1991**, *113*, 1786 and references therein.

(3) The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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Scheme I

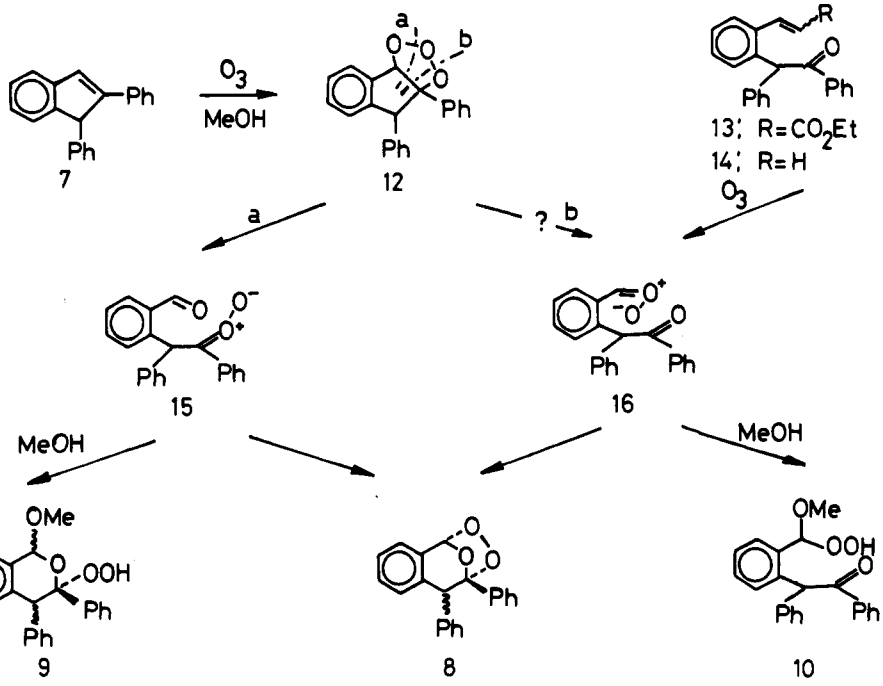


Table I. Ozonolysis of 1,2-Diphenylindene (7) and Keto Olefins 13 and 14[a]

substr	solvent	reaction temp, °C	products: ozonide 8 % yield	ozonide 8 exo/endo	others (% yield)
7	CCl_4	0	60	62:38	
7	CH_2Cl_2	−70	85	64:36	
7	$MeOH/CH_2Cl_2$ (1:1, v/v)	0	51	78:22	**9a** (29), **9b** (4)
7	$MeOH/CH_2Cl_2$	−70			**9a** (51)[b]
13	$MeOH/CH_2Cl_2$	0			**10** (45), **11** (45)
13	$MeOH/CH_2Cl_2$	−70			**10** (49), **11** (47)
14	CF_3CH_2OH/CH_2Cl_2 (1:1, v/v)	0	31	100:0	**11** (41)
14	$MeOH/CH_2Cl_2$	0	2	100:0	**10** (34), **11** (36)

[a] Reactions of 7, 13, and 14 with 1.5, 3, and 2 equiv of ozone, respectively. [b] Indene 7 was recovered in 40%.

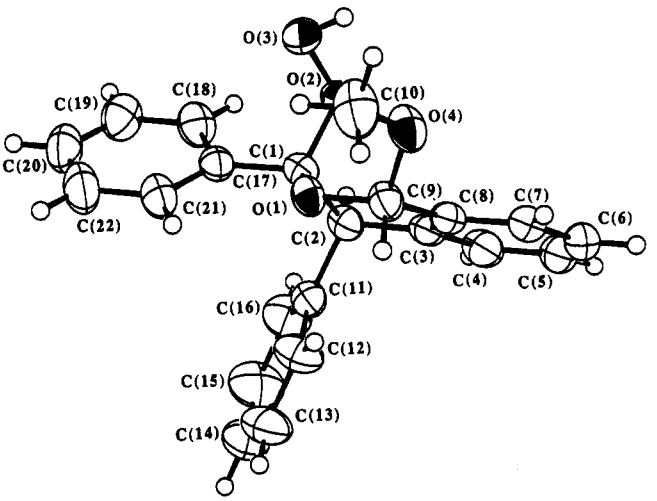


Figure 1. The molecular structure of isochroman *trans*-**9** (ORTEP,[14] 50% probability ellipsoids).

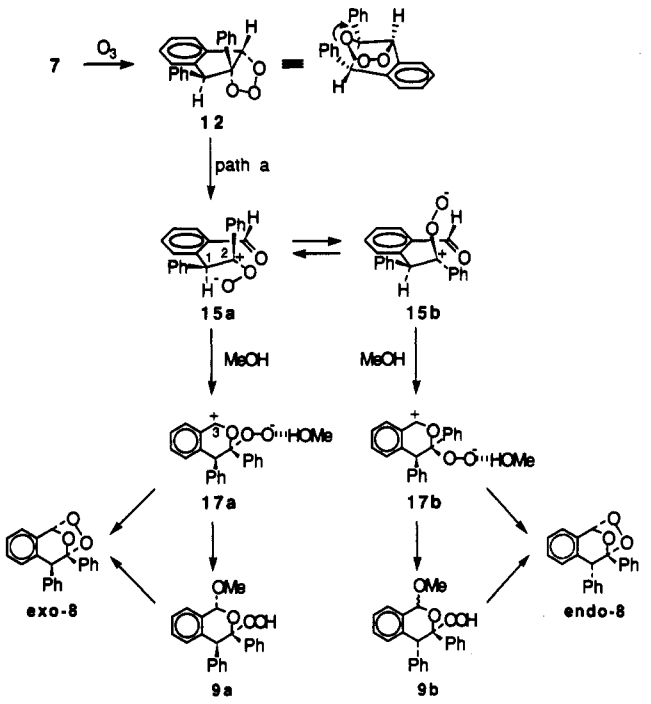
which the carbonyl oxide **16** is independently and unambiguously derived, in $MeOH/CH_2Cl_2$ at 0 or −70 °C yielded the α-methoxyalkyl hydroperoxide **10** in ca. 47% yield; keto olefin **14** afforded a similar result. Thus, the absence of the hydroperoxide **10** as the major component of the product mixture from the ozonolysis of **7** under the similar conditions (Scheme I and Table I) tends to suggest that the PO **12** does not decompose via path b (Scheme I) to any significant extent. It is noteworthy that in the case of 1,2,3-triphenylindene (**1**), fragmentation of the corresponding PO is also highly regioselective, as demonstrated by the exclusive formation of **3** via the carbonyl oxide intermediate **35** (Scheme IV).

Although the formation of each of the monomeric ozonolysis products, viz. ozonides **8** and isochromans **9**, can be understood in terms of an overall mechanism involving the conventional ozonolysis intermediate **15** (Scheme I),[4a,b] the effect of the reaction temperature on the composition of the product mixtures would require some explanation. As a consequence of the sterically congested nature of indene **7**, approach of ozone should be restricted to the least hindered face of the olefinic double bond (Scheme II). Thus, concerted cycloaddition of ozone with retention of configuration would give the corresponding PO **12**, which on subsequent selective cycloreversion, would provide the key carbonyl oxide intermediate **15a**.

In a $MeOH/CH_2Cl_2$ solvent system, solvation of the carbonyl oxide moiety of this intermediate **15a** should enhance the electrophilicity of carbon atom C-2, facilitating

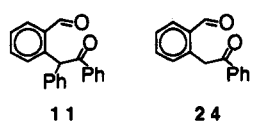
(4) For the leading references on alkene ozonolysis particularly in participating solvents, see: (a) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, Vol. 1, 1978; Vol. 2, 1982. (b) Bunnelle, W. H. *Chem. Rev.* **1991**, *91*, 335. (c) Kuczkowski, R. L. In *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI Press: Greenwich, 1991; Vol. 3. (d) Griesbaum, K.; Kiesel, G. *Chem. Ber.* **1989**, *122*, 145. (e) Paryzek, Z.; Martynow, J.; Swoboda, W. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1222. (f) Bunnelle, W. H.; Isbell, T. A. *J. Org. Chem.* **1992**, *57*, 729. (g) Nakamura, N.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1987**, *109*, 4969. (h) Bunnelle, W. H.; Lee, S.-G. *J. Am. Chem. Soc.* **1992**, *114*, 7577.

Scheme II



its partial capture by the oxygen atom of the adjacent carbonyl group to give the pivotal intermediate **17a** (Scheme II). Subsequent competition between the pendent peroxy group and methanol for the capture of the carbocation center at C-3 of **17** would yield either the *exo*-ozonide *exo*-**8** or the methanol-derived product **9a**, respectively. At lower temperatures, where solvent effects are more pronounced, solvent capture appears to be more highly favored at the expense of intramolecular cyclization. As the temperature is increased, however, the latter process becomes increasingly important. In the case of the sterically more-congested 1,2,3-triphenylindene (**1**), however, formation of the isochroman derivative **3** predominates irrespective of the reaction temperature.[2a]

Ozonization of **7** in $MeOH/CH_2Cl_2$ at 0 °C provided the usual *exo*–*endo*-ozonides **8** and the isochroman derivative **9a**, together with a small but significant quantity of the isomeric methanol-participated product **9b** (4% yield). In addition, the exo/endo ratio of ozonide **8** was 78:22, whereas the ratio of the isochromans **9a**/**9b** was 29:4, suggesting that ozonide formation is a less stereoselectivity process. Consistent with this, the exo/endo ratio of the ozonide **8** can be as low as 3:2 in the reactions in aprotic solvents such as CCl_4 at 0 °C or in CH_2Cl_2 at −70 °C, in which the carbonyl oxide intermediate **15** is likely to be weakly solvated (Table I). In this respect, it is worth noting that the ozonolysis of keto olefin **14** in CF_3CH_2OH/CH_2Cl_2 at 0 °C gave only *exo*-**8** (31%) together with **11** (41%).



If the attack of ozone on indene **7** at 0 °C retains a similar degree of facial selectivity, then the formation of **9b** in $MeOH/CH_2Cl_2$ implies that some conversion of the weakly-solvated **15a** to the rotameric **15b** must occur to some extent (Scheme II). In nonpolar aprotic solvents, interconversion between two rotamers, **15a** and **15b**, would be expected to occur more easily, and as a result, *endo*-**8** would be produced in substantial amounts, although *exo*-**8** would still be the major stereoisomer.

Ozonolysis of 2-Phenylindene (18). Ozonolyses of **18** were carried out in $MeOH/CH_2Cl_2$ at 0 and −70 °C (Scheme III and Table II). The resulting product mixtures were considerably more complex than those obtained from 1,2-diphenylindene (**7**). In addition to 2-phenylindene ozonide (**19**) and 2-(*o*-formylphenyl)-1-phenylethanone (**24**), four isomeric methanol-derived products were obtained.

Repeated column chromatography of this mixture of methanol-derived products on silica gel (elution with a mixture of ether and benzene) gave three main fractions: the isochroman derivative **20** (^1H NMR δ 9.04, OO*H*), followed by an equilibrating mixture of the cyclic hemiperacetal **22** and the methoxyalkyl hydroperoxide **23**,[4d,f] and finally the isomeric hemiperacetal **21** (^1H NMR δ 3.60, O*H*[2]).

The following results provide additional support for the structural assignments of the methanol-derived products **20**–**23**. Under similar conditions, ozonolysis of the keto olefin **26**, from which the carbonyl oxide intermediate **28** may be selectively derived, yielded a mixture of **22** and **23** in a ratio of ca. 1:1 (Scheme III and Table II). Second, consistent with the hemiperacetal structure of **21** and **22**, treatment of either **21** or a mixture of **22** and **23** with trifluoroacetic acid in methanol afforded the same dimethoxy-substituted dioxepane **30**. Finally, the reaction of the isochroman derivative **20** with trifluoroacetic acid in methanol under similar conditions resulted in the elimination of hydrogen peroxide with the formation of vinyl ether **31**.

The yield of ozonide **19** was found to increase significantly at higher temperature (17% at −70 °C; 53% at 0 °C), with concomitant decreases in the yields of both isochroman **20** (19% at −70 °C; 13% at 0 °C) and hemiperacetal **21** (12% at −70 °C; 6% at 0 °C). In contrast, the yield of the mixture of **22** and **23** showed little change with the reaction temperature (9% at −70 °C; 12% at 0 °C).[5]

These results can be rationalized in terms of a mechanism illustrated in Scheme III. The formation of four methanol-derived products **20**–**23** clearly demonstrates that in the case of the PO **25**, both possible modes of cycloreversion (paths c and d) are in operation, yielding the carbonyl oxide intermediates **27** and **28**, respectively. The more sterically congested ketone *O*-oxide **27** leads to the formation of ozonide **19** and two methanol-derived products, **20** and **21**; at −70 °C capture by methanol predominates, while at 0 °C ozonide formation appears to be more favored. This trend is similar to that observed in the ozonolysis of 1,2-diphenylindene (**7**), 2,3-diphenylindene (**4**),[2b] 1-methyl-2,3-diphenylindene,[2b] and 1-phenylacenaphthylene.[6] In the case of the less-hindered aldehyde *O*-oxide **28**, however, capture by methanol yielding a mixture of **22** and **23** seems to be much faster than intramolecular cyclization with the adjacent ketonic carbonyl group leading to ozonide **19** since ozonolysis of keto olefin **26**, which can only produce peroxidic products via intermediate **28**, does not yield **19** in isolable quantities.

(5) The percent yields quoted are isolated yeilds; the starting material **18** was consumed completely at 0 °C, whereas at −70 °C 27% of unreacted **18** was recovered together with the reaction products **19**–**23**.

(6) Sugimoto, T.; Nojima, M.; Kusabayashi, S. *J. Org. Chem.* **1990**, *55*, 3816.

Scheme III

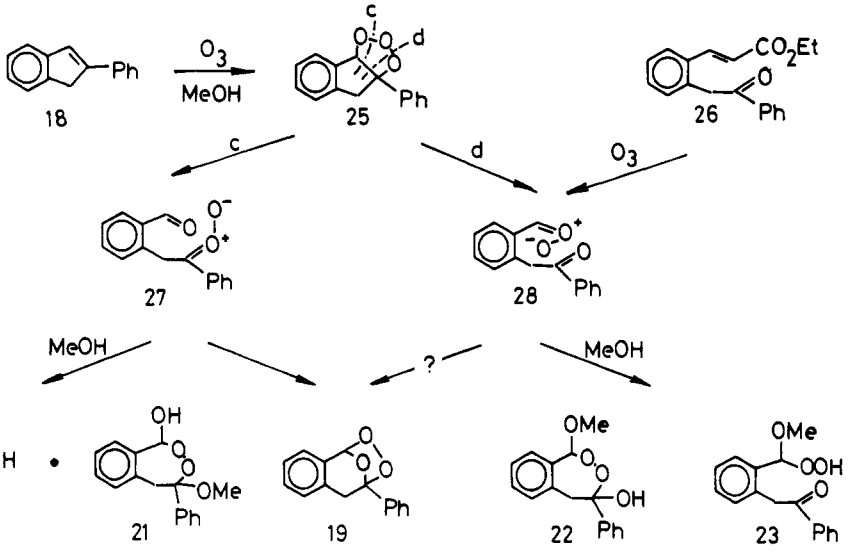


Table II. Ozonolysis of 2-Phenylindene (18) and Keto Olefins 26 and 32[a]

substr	solvent	reaction temp, °C	products (% yield)
18	CCl_4	0	19 (76)
18	$MeOH/CH_2Cl_2$ (1:1, v/v)	0	19 (53), 20 (13), 21 (6), 22 + 23 (12),[b] 24 (3)
18	$MeOH/CH_2Cl_2$	−70	19 (17), 20 (19), 21 (12), 22 + 23 (9),[b] 24 (9)[c]
26	CCl_4	0	24 + 29 (85)[d]
26	CF_3CH_2OH/CH_2Cl_2 (1:1, v/v)	−70	19 (14), 24 + 29 (35)[d]
26	$MeOH/CH_2Cl_2$	0	22 + 23 (50),[b] 24 + 29 (35)[d]
26	$MeOH/CH_2Cl_2$	−70	22 + 23 (54),[b] 24 + 29 (25)[d]
32	Et_2O	0	24 (47), 33 (38)
32	CF_3CH_2OH/CH_2Cl_2	0	19 (24), 24 (41), 33 (16)
32	$MeOH/CH_2Cl_2$	0	22 + 23 (62), 24 (33)

[a] Reactions of 18, 26, and 32 with 1.5, 3, and 1.5 equiv of ozone, respectively. [b] The 22/23 ratio was ca. 1:1. [c] Indene 18 was recovered in 27%. [d] The isolated yield; the ^1H NMR spectra of the crude products did not show 24. The 24/29 ratio of the isolated mixture was ca. 3:7.

The ozonolysis of keto olefin 32 produced very similar results (Table II).[7] These observations led us to deduce, on the basis of the yields of the methanol-derived products 22 and 23, that in the ozonolysis of 2-phenylindene (18), the contribution of path d in Scheme III is less than 30%.[8]

In summary, the results of this study suggest that the PO derived from 1,2-diphenylindene (7) decomposes in a highly selective fashion via path a (Scheme I). Although the ozonolysis of 2-phenylindene (18) also proceeds mainly in a similar manner (path c, Scheme III), the alternative scission pathway d (Scheme III) also makes a significant contribution to the overall reaction mechanism. The difference in selectivity between these two systems is considered to be related to their respective substitution patterns.

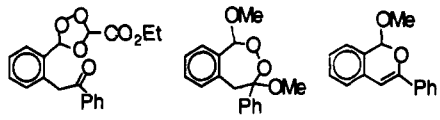
From consideration of the putative structure of the 1-phenylindene PO, the solitary phenyl group at C-1 would be expected to exert only a minimal steric effect on the atoms of the 1,2,3-trioxolane ring of the PO and hence on the selectivity of the subsequent ring cleavage process. Some support for this notion comes from the experimental observation that the ozonolysis product mixtures from indene and the 1-phenyl derivative respectively were found to be similar in terms of composition.[9] In the PO derived from 2-phenylindene 25, the absence of a bulky substituent at C-1 means that the phenyl group can readily undergo rotation about the C–C bond and hence minimize steric interactions with neighboring substituents. Consequently, although the C-2 phenyl group is located at the bridgehead position in PO 25, any steric effect on the subsequent cycloreversion process is likely to be diminished.

On the other hand, the vicinal phenyl groups at C-1 and C-2 in PO 12 would be most likely to adopt conformations in which their ring planes were stacked roughly parallel with respect to each other and angled substantially out of the normal plane of the indene plane. Such arrangements would necessarily result in increased steric interactions between the C-2 phenyl group and the nearest atom of the 1,2,3-trioxolane ring in PO 12 as compared to those envisaged in PO 25. This inherent steric compression in PO 12 would then be relieved if the cycloreversion process were to follow a mechanistic sequence analogous to that proposed by Kuczkowski,[4c] viz. that, in the transition state of this process, as the central oxygen atom moves out of the plane of the 1,2,3-trioxolane, there should be simultaneous and substantial movement of the substituent attached to the carbonyl oxide carbon. As a consequence, the scission pathway a (Scheme II) leading to carbonyl oxide 15a should be favored over the alternative one leading to 15b.

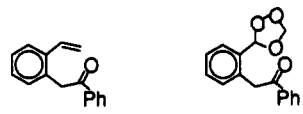
(7) Keto olefins 26 and 32 produce ozonides 29 and 33 which arise from direct recombination of the respective initially formed carbonyl oxide/carbonyl pair(s). Although two carbonyl oxide/carbonyl pairs could be obtained in principle in each case, the relative contributions of each cannot be inferred on the basis of the structures of the ozonides 29 and 33.

(8) In this discussion, there is an implicit assumption that the carbonyl oxide 28, irrespective of whether it had been derived from indene 18 or the acyclic keto olefins 26 and 32, should have similar reactivity. If the carbonyl oxide 28 derived from indene 18 were generated predominantly as the syn geometrical isomer, an arrangement considered to be more favorable toward intramolecular cyclization, the formation of ozonide 19 would compete more efficiently against the solvent capture processes which produce 22 and 23.[4h] In this case, the contribution of path d in Scheme III would need to be revised upward from the estimated value of 30%, though it would be less than 50% (in the reaction of 18 at −70 °C, (20 + 21)/(19 + 22 + 23) = 31:26).

(9) As judged from the composition of the solvent-derived products, the ozonolyses of indene and of 1-phenylindene were found to produce in each case both possible carbonyl oxide/carbonyl pairs in roughly equal quantities: Teshima, K.; Nojima, M. Unpublished results.



29 30 31



32 33

Although the ozonolysis of 2,3-diphenylindene (4) produced the hemiperacetal 6, necessarily derived from carbonyl oxide 34 (eq 2)[2b] as the sole methanol-derived product, the results above for indene 18 raise the question as to whether the primary ozonide derived from 4 may also decompose by both possible modes. Our attempts to resolve this question have been rendered, thusfar, inconclusive because ozonolysis of keto olefins 38 and 39 in $MeOH/CH_2Cl_2$ gave relatively small quantities of ozonide 5 (ca. 10–15%) together with nonperoxidic products such as partial-cleavage products 41 and 42, respectively,[4g,10] and keto aldehyde 44 (Scheme IV and Table III). When ozonolysis of keto olefin 40 was also conducted in the presence of protic solvents CF_3CH_2OH or MeOH, the major products obtained were again the partial-cleavage product 43 and diketone 45; no solvent-participated products derived from the carbonyl oxide intermediate 37 were observed (Table III).

Experimental Section

General. ^1H- and ^{13}C-NMR spectra were obtained with a JNM-PS-100 and JNM-GSX-400 instruments. Unless otherwise mentioned the spectra were recorded in $CDCl_3$. Ozonolyses were carried out with a Nippon Ozone Model 0-1-2 ozonator; dry oxygen containing about 2% of ozone was introduced at a speed of 50 L/h in the solution of a substrate. 1,2-Diphenylindene (7)[11] and 2-phenylindene (18)[12] were prepared by the reported methods. 7: mp 177 °C (from ethanol); ^1H NMR δ 4.96 (s, 1 H), 6.9–7.5 (m, 15 H). 18: mp 159–161 °C (from hexane); ^1H NMR δ 3.77 (s, 2 H), 7.0–7.7 (m, 10 H). Ethyl 2-(phenylbenzoylmethyl)-cinnamate (13) and ethyl 2-(benzoylmethyl)cinnamate (26) were prepared from the reaction of the corresponding keto aldehydes, 11 and 24, and (carbethoxymethylene)triphenylphosphorane by a standard method.[13] 13: mp 129–130 °C (from CH_2Cl_2–hexane); IR 1705, 1680, 1270 cm^{-1}; ^1H NMR δ 1.24 (t, J = 7 Hz, 3 H), 4.21 (q, J = 7 Hz, 2 H), 6.32 (s, 1 H), 6.32 (d, J = 16 Hz, 1 H), 7.0–8.1 (m, 15 H). Anal. Calcd for $C_{25}H_{22}O_3$: C, 81.06; H, 5.99. Found: C, 81.19; H, 5.92. 26: mp 83.0–83.5 °C (from ethyl acetate–hexane); IR 1705, 1680, 1630, 1315, 1180 cm^{-1}; ^1H NMR δ 1.28 (t, J = 7 Hz, 3 H), 4.24 (q, J = 7 Hz, 2 H), 4.49 (s, 2 H), 6.40 (d, J = 16 Hz, 1 H), 7.2–8.1 (m, 9 H), 7.98 (d, J = 16 Hz, 1 H). Anal. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.26; H, 6.19. The reactions of diketones 11, 24, 44, and 45 and methylenetriphenylphosphorane gave in each case the corresponding keto olefins 14, 32, 39, and 40, respectively. 2-(o-Ethenylphenyl)-1,2-diphenylethanone (14): mp 78–79 °C (from hexane); ^1H NMR (CCl_4) δ 5.30 (dd, J = 11 and 2 Hz, 1 H), 5.58 (dd, J = 20 and 2 Hz, 1 H), 6.18 (s, 1 H), 7.02 (dd, J = 11 and 20 Hz, 1 H), 7.0–7.6 (m, 12 H), 7.7–8.0 (m, 2 H); IR 1685, 1600, 1205, 990, 735 cm^{-1}. Anal. Calcd for $C_{22}H_{18}O$: C, 88.59; H, 6.05. Found: C, 89.01; H, 5.87. 2-(o-Ethylphenyl)-1-phenylethanone (32): mp 141–143 °C (from hexane); ^1H NMR δ 4.20 (s, 2 H), 5.22 (br d, J = 11 Hz, 1 H), 5.50 (br d, J = 17 Hz, 1 H), 6.83 (dd, J = 11 and 17 Hz, 1 H), 6.9–7.5 (m, 7 H), 7.5–8.0 (m, 2 H); IR 3060, 1685, 1200, 985, 750 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O$: C, 86.44; H, 6.36. Found: C, 86.00; H, 6.36. 2-[o-(1-Phenylethenyl)phenyl]-1-phenylethanone (39): an oil; ^1H NMR (CCl_4) δ 3.95 (s, 2 H), 5.17 (d, J = 1 Hz, 1 H), 5.70 (d, J = 1 Hz, 1 H), 7.1–7.5 (m, 12 H), 7.6–7.8 (m, 2 H); ^{13}C NMR δ 43.10, 115.90, 126.61–148.57 (19 C), 197.73; IR 1690, 1330, 1210, 755, 685 cm^{-1}; MS m/e 298 (M^+). Anal. Calcd for $C_{22}H_{18}O$: C, 88.55; H, 6.09. Found: C, 88.56; H, 6.17. 2-[o-(1-Phenylethenyl)phenyl]-1,2-diphenylethanone (40): mp 141–143 °C (from methanol); ^1H NMR (CCl_4) δ 5.07 (d, J = 2 Hz, 1 H), 5.70 (d, J = 2 Hz, 1 H), 5.92 (s, 1 H), 6.9–7.7 (m, 19 H); IR 1685, 1450, 1220, 700 cm^{-1}. Anal. Calcd for $C_{28}H_{22}O$: C, 89.80; H, 5.93. Found: C, 89.80; H, 5.90.

Ozonolysis of 1,2-Diphenylindene (7) in $MeOH/CH_2Cl_2$ at 0 °C. Through a solution of 7 (2 mmol) in $MeOH/CH_2Cl_2$ (40 mL, 1:1) was passed a slow stream of ozone (3 mmol) at 0 °C. Then the mixture was poured into ice-cold, aqueous KH_2PO_4, and the products were extracted with ether. The organic layer was separated and dried ($MgSO_4$), and the solvent was removed under vacuum. Column chromatography of the residue on silica gel (elution with benzene–hexane, 1:1) gave a mixture of *exo*- and *endo*-1,2-diphenylindene ozonides (8), which could be separated from each other by repeated column chromatography. *exo*-8: mp 150–151 °C (from methanol); ^1H NMR δ 4.50 (s, 1 H), 6.65 (s, 1 H), 6.7–7.3 (m, 14 H). Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.67; H, 5.19. *endo*-8: mp 133–134 °C (from methanol); ^1H NMR δ 4.76 (s, 1 H), 6.56 (s, 1 H), 6.7–7.3 (m, 14 H). Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.73; H, 5.13. From the second fraction (elution with ether–benzene, 1:99) was isolated (3α,4α)-3,4-dihydro-1-methoxy-3,4-diphenyl-1*H*-2-benzopyran-3-yl hydroperoxide (9b): mp 138–140 °C (from ethyl acetate–hexane); IR 3420, 1450, 1360, 1240, 1080, 1020 cm^{-1}; ^1H NMR δ 3.85 (s, 3 H), 4.33 (s, 1 H), 5.90 (s, 1 H), 6.6–7.5 (m, 14 H), 9.30 (s, 1 H). Anal. Calcd for $C_{22}H_{20}O_4$; C, 75.84; H, 5.79. Found: C, 75.70; H, 5.86. The final fraction (elution with ether–benzene, 1:50) contained (1α,3α,4α)-3,4-dihydro-1-methoxy-3,4-diphenyl-1*H*-2-benzopyran-3-yl hydroperoxide (9a): mp 160–162 °C (from ethyl acetate–hexane); IR 3400, 1450, 1360, 1230, 1040 cm^{-1}; ^1H NMR δ 3.86 (s, 3H), 4.19 (s, 1 H), 6.03 (s, 1H), 6.5–7.4 (m, 14 H), 9.15 (s, 1 H). Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.85; H, 5.75. Found: C, 75.78; H, 5.76. Treatment of 9a (0.3 mmol) with 1 equiv of trifluoroacetic acid in CH_2Cl_2 (10 mL) at rt for 15 h gave the *exo*-8 in 95% yield. Under similar conditions 85% yield of *endo*-8 was obtained from 9b.

X-ray Crystal Structure Determination of the Isochroman 9a. A single crystal of 9a (from ethyl acetate–hexane) was subjected to X-ray crystallographic analysis. Full experimental details with the crystal data from 9a are in the supplementary material.

Ozonolysis of Keto Olefin 13 in $MeOH/CH_2Cl_2$ at −70 °C. Keto olefin 13 (1 mmol) was treated with 3 equiv of ozone in $MeOH/CH_2Cl_2$ (30 mL, 1:1) at −70 °C. After workup as above, the crude products were column chromatographed on silica gel. Elution with ether–benzene (1:50) gave 2-(o-formylphenyl)-1,2-diphenylethanone (11): mp 119–120 °C (from ethyl acetate); IR 1690, 1695 cm^{-1}; ^1H NMR δ 7.0–8.0 (m, 15 H), 10.04 (s, 1 H). Anal. Calcd for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37. Found: C, 84.37; H, 5.35. Subsequent elution with ether–benzene (1:9) yielded 2-[o-methoxyhydroperoxymethyl)phenyl]-1,2-diphenylethanone (10): mp 133–136 °C (from ethyl acetate–hexane); IR 3350, 1670, 1450, 1200, 1070, 1000 cm^{-1}; ^1H NMR δ 3.46 (s, 3 H) 5.75 (s, 1 H), 6.64 (s, 1 H), 7.0–8.0 (m, 14 H), 8.30 (s, 1 H). Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 75.90; H, 5.67.

Ozonolysis of 2-Phenylindene (18) in $MeOH/CH_2Cl_2$ at −70 °C. Reaction of 18 (2 mmol) in $MeOH/CH_2Cl_2$ (30 mL, 1:1) with ozone (3 mmol) was undertaken at −70 °C. After workup, the products were separated by column chromatography on silica gel. From the first fraction (elution with benzene–hexane, 1:4), the unreacted 18 was obtained. The second fraction (elution with benzene–hexane, 1:1) gave 2-phenylindene ozonide (19): mp 101–103 °C (from methanol); ^1H NMR δ 3.38 (d, J = 17 Hz, 1 H), 3.56 (d, J = 17 Hz, 1 H), 6.45 (s, 1 H), 6.7–7.1 (m, 9 H). Anal.

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Scheme IV

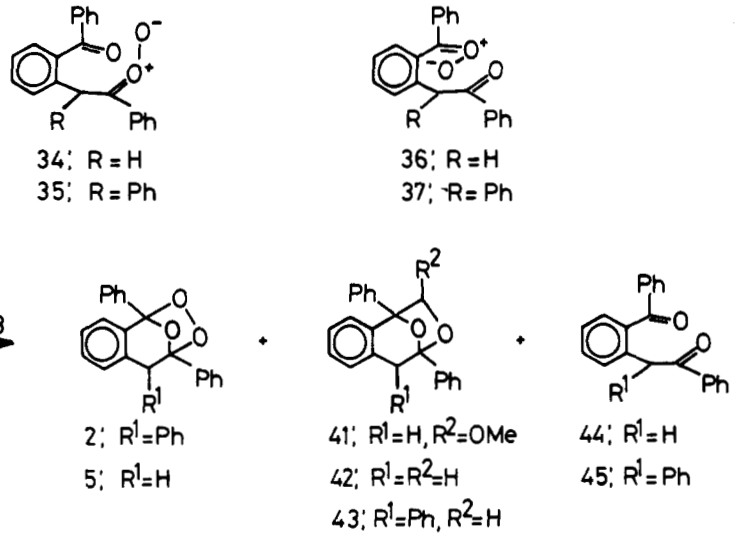

Table III. Ozonolysis of Keto Olefins 38, 39, and 40[a]

substr	solvent	reaction temp, °C	products (% yield)
38	CCl_4	0	5 (15), 41 (40)[b]
38	$MeOH/CH_2Cl_2$ (1:1, v/v)	−70	5 (14), 41 (41)[b]
39	CH_2Cl_2	−70	5 (38), 42 (7), 44 (34)
39	$MeOH/CH_2Cl_2$	−70	5 (11), 42 (11), 44 (69)
40	CF_3CH_2OH/CH_2Cl_2 (1:1, v/v)	0	2 (10),[c] 43 (34), 45 (26)
40	$MeOH/CH_2Cl_2$	0	43 (21), 45 (66)

[a] Reactions of 38, 39, and 40 with 1.5, 1.5, and 2 equiv of ozone, respectively. [b] Taken from the data in ref 4g. [c] The exo/endo ratio is 1:6.

Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 74.91; H, 5.04. From the third fraction (elution with ether–benzene, 1:99) was obtained 3,4-dihydro-1-methoxy-3-phenyl-1*H*-2-benzopyran-3-yl hydroperoxide (**20**): mp 95–96 °C; IR 3400, 1370, 1240, 1050, 1010 cm^{-1}; ^1H NMR δ 3.10 (s, 1 H), 3.72 (s, 3 H), 5.77 (s, 1 H), 6.9–7.7 (m, 9 H), 9.04 (s, 1 H). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.59; H, 5.96. The fourth fraction (elution with ether–benzene, 1:50) contained 2-(*o*-formylphenyl)-1-phenylethanone (**24**): mp 93–95 °C (from ethyl acetate–hexane); IR 1685, 1695 cm^{-1}; ^1H NMR δ 4.76 (s, 2 H), 7.2–8.1 (m, 9 H), 10.01 (s, 1 H). Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.39; H, 5.35. From the fifth fraction was obtained a ca. 1:1 mixture of 3-methoxy-7-hydroxy-7-phenyl-4,5-benzo-1,2-dioxepane (**22**) and 2-[*o*-(methoxyhydroperoxymethyl)phenyl]-1-phenylethanone (**23**): an oil; ^1H NMR δ 2.71 (d, J = 14 Hz, 1 H, **22**), 3.51 (s, 3 H, **22**), 3.63 (s, 3 H, **21**), 4.05 (d, J = 14 Hz, 1 H, **22**), 4.73 (s, 2 H, **23**), 5.56 (s, 1 H, **22**), 5.94 (s, 1 H, **23**), 6.9–8.0 (m, aromatic protons), 8.79 (s, 1 H, **23**). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.90; H, 6.02. The final fraction (elution with ether–benzene, 1:9) contained 3-hydroxy-7-methoxy-7-phenyl-4,5-benzo-1,2-dioxepane (**21**): an oil; ^1H NMR δ 2.67 (d, J = 14 Hz, 1 H), 3.21 (s, 3 H), 3.60 (br s, 1 H, H–D exchange in D_2O), 4.04 (d, J = 14 Hz, 1 H), 6.39 (s, 1 H), 6.47 (d, J = 7 Hz, 1 H), 6.9–7.7 (m, 7 H), 7.72 (d, J = 7 Hz, 1 H). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C 70.70; H, 5.88.

Ozonolysis of Keto Olefin 26 in CCl_4. Keto olefin **26** (1 mmol) was treated with 3 mmol of ozone in CCl_4 (30 mL) at 0 °C. After evaporation of the solvent, the ^1H NMR spectrum of the crude products was measured, which showed the formation of 3-(ethoxycarbonyl)-5-((*o*-benzoylmethyl)phenyl)-1,2,4-trioxolane (**29**) (a mixture of two stereoisomers, the ratio being around 2:1) almost quantitatively. **29**: an oil; ^1H NMR δ 1.27 (t, J = 7 Hz, 3 H), 4.22 (q, J = 7 Hz, 2 H), 4.37 (s, 2 H, minor), 4.39 (s, 2 H, major), 5.50 (s, 1 H, major), 5.61 (s, 1 H, minor), 6.14 (s, 1 H, minor), 6.43 (s, 1 H, major), 7.0–8.0 (m, 9 H). Because of the lability on silica gel (YMC, 70–230 mesh),[4] the column chromatography resulted in the isolation of a mixture of **29** and the keto aldehyde **24**, the ratio being around 7:3.

Ozonolysis of Keto Olefin 26 in $MeOH/CH_2Cl_2$ at −70 °C. A solution of **26** (1 mmol) in $MeOH/CH_2Cl_2$ (30 mL, 1:1) was treated with 3 mmol of ozone at −70 °C. After workup, the products were column chromatographed on silica gel. Elution with ether–benzene (1:99) gave a 3:7 mixture of keto aldehyde **24** and the normal ozonide **29** (25% yield). By subsequent elution with ether–benzene (1:9), a 1:1 mixture of the hemiperacetal **22** and the α-methoxyalkyl hydroperoxide **23** was obtained in 54% yield.

Treatment of a Isochroman Derivative 20 with Trifluoroacetic Acid in MeOH. A solution of an equimolar mixture of **20** and trifluoroacetic acid (0.5 mmol for each) in MeOH (20 mL) was kept with stirring at rt for 24 h. By column chromatography on silica gel (elution with benzene–hexane, 1:1) was obtained a 75% yield of 1-methoxy-4-phenyl-1*H*-2-benzopyran (**31**): an oil; ^1H NMR (CCl_4) δ 3.57 (s, 3 H), 6.11 (s, 1 H), 6.57 (s, 1 H), 6.9–7.9 (m, 9 H); MS m/e 238 (M^+). Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.67; H, 5.90. Found: C, 80.75; H, 5.78.

Treatment of Hemiperacetal 21 or a Mixture of Hemiperacetal 22 and Methoxy Hydroperoxide 23 with Trifluoroacetic Acid in MeOH. A solution of **21** (1 mmol) and trifluoroacetic acid (1 mmol) in MeOH (20 mL) was kept with stirring at rt for 24 h. By column chromatography on silica gel (elution with benzene–hexane 1:1) was obtained an 82% yield of 3,7-dimethoxy-7-phenyl-4,5-benzo-1,2-dioxepane (**30**): mp 109–111 °C (from methanol); ^1H NMR δ 2.77 (d, J = 14 Hz, 1H), 3.29 (s, 3 H), 3.73 (s, 3 H), 4.06 (d, J = 14 Hz, 1 H), 6.04 (s, 1 H), 6.50 (d, J = 7 Hz, 1 H), 6.9–7.4 (m, 7 H), 7.49 (d, J = 7 Hz, 1 H). Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.33; H, 6.29. Found: C, 71.06; H, 6.28. Treatment of a 1:1 mixture of **22** and **23** (1 mmol) with trifluoroacetic acid (1 mmol) in methanol under similar conditions yielded the same hemiperacetal **30** in 70% yield.

Ozonolysis of Keto Olefin 32 in CF_3CH_2OH/CH_2Cl_2. Ozonolysis of **32** (222 mg, 1 mmol) was conducted in CF_3CH_2OH/CH_2Cl_2 (15 mL) at 0 °C. The products were separated by column chromatography on silica gel. Elution with benzene–hexane (1:1) gave **19** (58 mg, 24%). Elution with benzene gave keto ozonide **33** (41 mg, 16%): an oil; ^1H NMR (CCl_4) δ 4.37 (s, 2 H), 5.16 (s, 1 H), 5.26 (s, 1 H), 6.10 (s, 1 H), 7.0–8.0 (m, 9 H); IR 1690, 1330, 1210, 1060 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.15; H, 5.35. Elution with benzene–ether (10.1) gave keto aldehyde **24** (92 mg, 41%).

Ozonolysis of Keto Olefin 39 in CH_2Cl_2. A CH_2Cl_2 solution (15 mL) of **39** (298 mg, 1 mmol) was treated with 2 equiv of ozone at −70 °C. After evaporation of the solvent, the products were separated by column chromatography on silica gel. Elution with benzene–hexane (5:1) gave 1,5-diphenyl-2,3-benzo-6,8-dioxabicyclo[3.2.1]octane (**42**) (22 mg, 7%): mp 141–142 °C (from

ether–hexane); ^{1}H NMR δ 3.30 (d, J = 17 Hz, 1 H), 3.66 (d, J = 17 Hz, 1 H), 4.25 (d, J = 6 Hz, 1 H), 4.55 (d, J = 6 Hz, 1 H), 7.0–8.0 (m, 14 H). Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.07; H, 5.78. Found: C, 84.26; H, 5.78. From the second fraction (benzene–hexane, 1:1) was obtained **5** (120 mg, 38%): mp 119 °C.[2b] Elution with benzene gave diketone **44** (102 mg, 34%): mp 67–68 °C.[2b]

Ozonolysis of Keto Olefin 40 in CF_3CH_2OH/CH_2Cl_2. To a solution of **40** (374 mg, 1 mmol) in CF_3CH_2OH/CH_2Cl_2 (15 mL, 1:1) was passed a slow stream of ozone (2 mmol) at 0 °C. The products were separated by column chromatography on silica gel. The first fraction (elution with benzene–hexane, 5:1) contained 1,4,5-triphenyl-2,3-benzo-6,8-dioxabicyclo[3.2.1]octane (**43**) (133 mg, 34%): mp 171–173 °C (from methanol); ^{1}H NMR δ 4.65 (s, 1 H), 4.70 (s, 1 H), 4.82 (s, 1 H), 6.8–7.7 (m, 19 H); IR 1500, 1100, 1010, 750, 690 cm^{-1}; MS m/e 390 (M^+). From the second fraction (benzene–hexane, 1:1) was obtained a mixture of *exo*- and *endo*- **2**[2a] (39 mg, 10%, exo/endo = 1:6). Elution with benzene gave diketone **44**[2a] (98 mg, 26%).

Supplementary Material Available: Details of the X-ray crystal structure determination of isochroman *trans*-**9** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.