Transannular Ozonides of 9-Alkoxyanthracenes

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Ozonation of 9-alkoxyanthracenes in methanol at −78 °C leads to transannular ozonides **7**, most of which can be isolated in crystalline form. On warming in CH_2Cl_2, ozonides **7** undergo around −30 °C a decomposition with O_2 release leading mainly to 10-alkoxy-9-anthrones **8**. The radical character of this decomposition is established, in the case of 9-methoxy-10-methylanthracene ozonide (**7e**), by adding H donors such as 2,4,6-tri-*tert*-butylphenol or hydroquinone, which direct the process toward the formation of 10-hydroperoxy-10-methyl-9-anthrone (**2a**).

A limited number of primary ozonides are known,[1a] and the transannular ozonides of anthracene derivatives which can be isolated at low temperature may be viewed as a particular class of such compounds. The study of their chemical behavior is therefore of interest.[1b,2]

Previously ozonides obtained from anthracenic *hydrocarbons* **1a–d** have been studied from this point of view, and it has been established that *meso*-dialkylated ozonides such as **1b,c** rearrange readily to 10-alkyl-10-(alkyldioxy)-9-anthrones **2b,c**. Originally found for **1b** which leads quite quantitatively to **2b** in CD_2Cl_2 at ambient temperature,[3a] this unexpected rearrangement has been confirmed recently with the more stable ozonide **1c** which affords **2c** in high yield on heating in $CDCl_3$.[3c] In the same way **1a** gives essentialy the hydroperoxide **2a**.[3b]

A different course of rearrangement takes place with ozonide **1d**, which bears a *meso*-phenyl group; this compound undergoes a migration of the phenyl substituent to oxygen followed by a major loss of O_2 ending in **3d**, or by a minor recombination to **4d**.[3b]

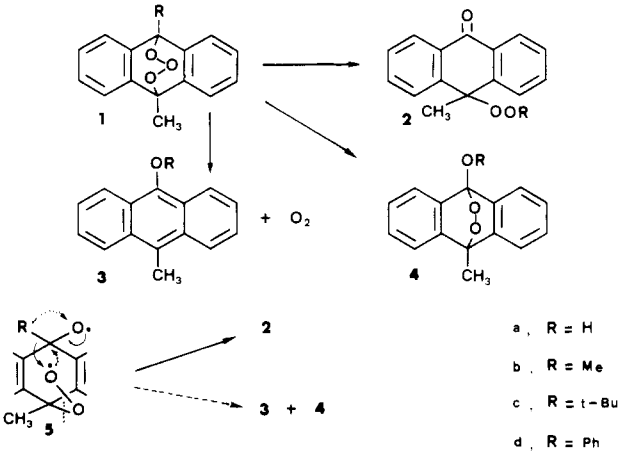
Though originally suspected to go intramolecularly through ionic intermediates, these rearrangements may well be rationalized by considering the possible transformations of a diradical **5** arising from a selective homolysis of one of the O–O bonds, which is reminiscent of the cleavage of di-*tert*-butyl trioxide[4] (Scheme I).

We report now the behavior of the transannular ozonides **7e–k** (see Table I) derived from *9-alkoxyanthracenes* **6e–k** along with trapping experiments establishing the radical nature of the observed reactions.

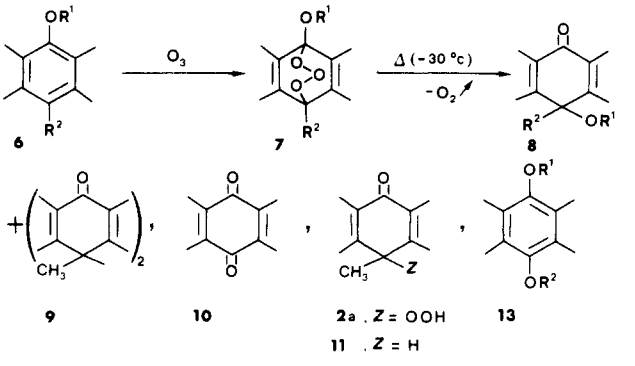
Results and Discussion

Ozonation of compounds **6e–k** in methanol (0.1 M) at −78 °C induces within 15 min the slow precipitation of colorless crystals of ozonides **7**, which after separation, washing with methanol, and drying, are isolated in yields approaching 50% (see Table I). This general procedure is applicable to most of the ozonides (**7e–g,j–k**) which are stable in the solid state at 0 °C or below for several hours,

Scheme I



Scheme II



or even days in the case of **7e**. For the purpose of their study these have been redissolved in CD_2Cl_2 at −78 °C. The less stable ozonides **7h,i** have been prepared and studied directly in solutions resulting from ozonation of **6h,i** in CD_2Cl_2 at −78 °C (Scheme II).

CD_2Cl_2 solutions of ozonides **7** are perfectly stable below −40 °C, and the recorded NMR spectra are fully consistent with the assigned epi-trioxide structures.[3d] They all undergo characteristic changes around −30 °C. A typical behavior is that of **7e**; as the temperature is raised, a rapid release of O_2 takes place while the solution becomes yellow. At −20 °C, no more gas is evolved, and the NMR spectrum of the colorless solution shows the presence of 10-methoxy-10-methyl-9-anthrone (**8e**) and, in minor proportions, of 10,10′-dimethyl-9-bianthrone (**9**) and anthraquinone (**10**).[5] After return to ambient temperature, these compounds can be separated by TLC on silica gel.

The same kind of decomposition is observed with most of the other ozonides leading mainly to the corresponding

(1) See: Bailey, P. S. In "Ozonation in Organic Chemistry"; Academic Press: New York, (a) 1978; Vol. I, p 15; 1982; (b) Vol. II, p 81.
(2) Erickson, R. E; Bailey, P. S.; Davies, J. C., Jr. *Tetrahedron* **1962**, *18*, 389.
(3) (a) Rigaudy, J.; Cuong, N. K.; Rothschild, J. F. *Tetrahedron Lett.* **1973**, 4439. (b) Rigaudy, J.; Cuong, N. K.; Albouy, J. P.; Chetrit, A. *Tetrahedron Lett.* **1976**, 1089. (c) Ito, Y.; Matsuura, A.; Otani, R.; Matsuura, T.; Fukuyama, K.; Katiube, Y. *J. Am. Chem. Soc.* **1983**, *105*, 5699. (d) Gobert, F.; Altenburger-Combrisson, S.; Albouy, J. P. *J. Org. Magn. Reson.* **1979**, *12*, 202.
(4) Bartlett, P. D.; Gunther, P. *J. Am. Chem. Soc.* **1966**, *88*, 3288.
(5) Formation of 9,10-epidioxy-9,10-dimethoxy-9,10-dihydroanthracene, deduced in ref 2 from the appearance of a signal at δ 3.70, is not detected. Moreover the methoxy peak of this endoperoxide is located at δ 4.03, as was checked on a sample prepared according to ref 9.

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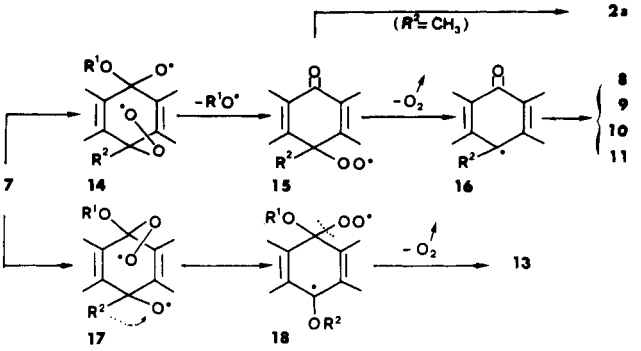
10-alkoxy-9-anthrones **8**, which can be isolated as above (see Table II). However a significant difference appears with ozonides **7f–h** which bear more complex alkoxy groups than methoxy; the formation of anthrones **8** is largely reduced or even suppressed to the benefit of that of **9** and of additional compounds, principally 10-methyl-9-anthrone (**11**) with **7f** and 10-hydroperoxy-10-methyl-9-anthrone (**2a**) with **7g** and **7h**. At the same time, one can detect by NMR the presence of alcohols and of carbonyl derivatives, i.e., acetaldehyde, acetone, and benzaldehyde, respectively, coming from the lost alkoxy substituents by hydrogen abstraction or dehydrogenation. Moreover, an unique behavior is shown by ozonide **7k** bearing a phenyl substituent; in this case a minor proportion of the rearranged diether **13k** is formed beside anthrone **8k**.

A likely mechanism accounting for the above results is shown in Scheme III. According to this mechanism a selective cleavage of the O(1)–O(2) bond of the ozonide **7** would lead to diradical **14**, which is able to undergo easily a further cleavage of the alkoxy radical $R^1O\cdot$, affording **15**. The subsequent fragmentation of **15** to O_2 and radical **16** is not surprising in view of the stabilization provided to **16** by delocalization. Radical **16** could then afford the anthrone **8** by recombining with radicals $R^1O\cdot$ or dimerize to **9**. Alternatively **15** and **16** could abstract hydrogen from the alkoxy radicals, leading to the aforementioned by-products.

Scheme III



We have been able to confirm the radical character of the decomposition by adding hydrogen donors to ozonide **7e** (see Table III). Alcohols are not very suitable for this

Table I. Yields and Physical Properties of Ozonides 7

ozonides 7			% yields of formation[a]	% isolated yields[b]	instantaneous dec temp, °C[c]	^{1}H NMR (CD_2Cl_2), δ (J, Hz)	
7	R^1	R^2				R^1	R^2
e	CH_3	CH_3	80	50	86–87	3.95 (s, 3 H)	2.13 (s, 3 H)
f	C_2H_5	CH_3	82	52	92–93	4.28 (q, 2 H, J = 7), 1.50 (t, 3 H, J = 7)	2.15 (s, 3 H)
g	$CH(CH_3)_2$	CH_3	82	53	99–100	4.67 (hept, 1 H, J = 6),[d] 1.40 (d, 3 H, J = 6), 1.58 (d, 3 H, J = 6)	2.08 (s, 3 H)
h	$CH_2C_6H_5$	CH_3	62			5.35 (s, 2 H)	2.12 (s, 3 H)
i	CH_3	H	67			3.93 (s, 3 H)	6.15 (s, 1 H)
j	CH_3	OCH_3	90	45	126–127	3.98 (s, 3 H)	3.98 (s, 3 H)
k	CH_3	C_6H_5	75	45	168–169	3.98 (s, 3 H)	≈7.50 (m, 5 H)

[a] Evaluated from integrated NMR signals of the ozonized solutions in CD_2Cl_2 at −60 °C. [b] Of crystalline ozonides isolated from methanolic solutions. [c] By projection onto a Köfler block. [d] Molecular asymmetry is revealed in NMR by the nonequivalent CH_3 groups.

Table II. Relative Proportions (±5%) of Decomposition Products of Ozonides 7, Estimated from Integrated ^{1}H NMR Signals of CD_2Cl_2 Solutions at Room Temperature

ozonides	8	9	10	11	12	13	2a	other detected compds[a]
7e	75	5	20					
7f	40	5	25	30				CH_3CH_2OH, CH_3CHO
7g[b]		30	25		10		20	$(CH_3)_2CHOH$, $(CH_3)_2C{=}O$
7h[c]		+	+		+		+	$C_6H_5CH_2OH$, C_6H_5CHO
7i	60		40					CH_3OH
7j	65		35					CH_3OH
7k	70		15			15		CH_3OH

[a] Proportions not determined. [b] Several nonidentified products were also present. [c] Several compounds were identified (+), but their relative proportions could not be evaluated precisely owing to the complexity of the reaction mixture.

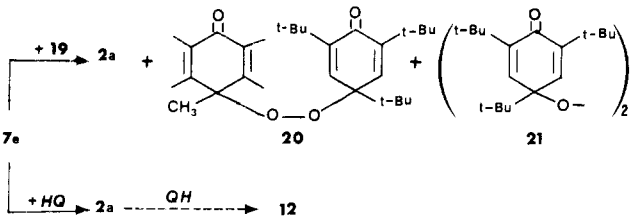
Table III. Yields (%) of Products Isolated by TLC after Decomposition of Ozonide 7e in the Presence of Added H Donors

added H donors	8e	8'e	8f	9	10	2a	12	20	21
In CD_2Cl_2									
none	50			15	21				
CD_3OD (10%)		64		2	5	5	9		
C_2H_5–OH (10%)			74		12	3	6		
$(CH_3)_2CHOH$ (10%)	18			18	38	15			
19 (1 mol)	40					13		26	
19 (4 mol)	27					25		41	3
In CD_2Cl_2/CD_3OD (1:1)									
HQ (2 mol)	7	16		9	7		48		
In CD_2Cl_2/CH_3CN (1:1)									
none	47			7	16				
HQ (2 mol)					4	82			

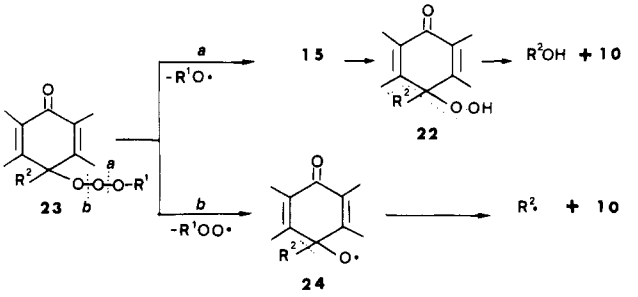
Table IV. ^{1}H NMR Data for 9-Alkoxyanthracenes 6

9-alkoxyanthracenes 6				^{1}H NMR (CD_2Cl_2), δ (J, Hz)	
6	R^1	R^2	ref	R^1	R^2
e	CH_3	CH_3	7b	4.12 (s, 3 H)	3.03 (s, 3 H)
f	CH_2CH_3	CH_3	10	4.18 (q, 2 H, J = 7), 1.55 (t, 3 H, J = 7)	2.95 (s, 3 H)
g	$CH(CH_3)_2$	CH_3		4.48 (hept, 1 H, J = 6), 1.33 (d, 6 H, J = 6)	2.88 (s, 3 H)
h	$CH_2C_6H_5$	CH_3		5.23 (s, 2 H)	3.05 (s, 3 H)
i	CH_3	H	8a	4.12 (s, 3 H)	
j	CH_3	OCH_3	9	4.20 (s, 3 H)	4.20 (s, 3 H)
k	CH_3	C_6H_5	8b	4.23 (s, 3 H)	

Scheme IV



Scheme V



purpose as they appear to react more or less rapidly with the ozonides themselves *in solution* around −30 °C, leading mainly to 10-alkoxy-9-anthrones with exchanged alkoxy groups. Thus, addition of 10% of CD_3OD or C_2H_5OH to ozonide **7e** in CH_2Cl_2 does not change the appearance of the decomposition but leads in high yields to anthrones **8'e** ($R^1 = CD_3$) or **8f**, instead of **8e**. As no exchange of methoxy group occurred when **8e** was treated with alcohols in these conditions, it is probable that the origin of **8'e** or **8f** is a solvolytic ring opening of ozonides **7** by alcohols. Yet the latter react partially as hydrogen donors since small proportions of hydroperoxide **2a** are also isolated. More conclusive results have been obtained with 2,4,6-tri-*tert*-butylphenol (**19**), which does not react with the ozonide (see Scheme IV). The blue color of the 2,4,6-tri-*tert*-butylphenoxyl radical develops at the start of the decomposition of **7e** at −30 °C and remains unchanged until the end of the O_2 release. From the products isolated afterwards, it appears that the normal reaction has been largely directed toward the formation of hydroperoxide **2a** and of the unsymmetrical peroxide **20**, two compounds which should arise from radical **15** or less probably from **14** owing to the rapid cleavage of the latter. A small amount of the symmetrical peroxide **21** of 2,4,6-tri-*tert*-butylphenoxyl is also obtained.

The use of hydroquinone (HQ) as the hydrogen donor is even more demonstrative of the intermediacy of **15** (or **14**). Added in CD_3OD prior to the decomposition, HQ leads in high yields to quinhydrone (QH) and to 10-hydroxy-10-methyl-9-anthrone (**12**) as hydroperoxide **2a** is reduced to **12** by quinhydrone under these conditions. But when HQ (2 mol) is added in CH_3CN, hydroperoxide **2a** becomes the almost exclusive reaction product since quinhydrone precipitates out as soon as quinone is formed.

Formation of appreciable proportions of anthraquinone **10** during the decomposition of ozonides **7** in the absence of hydrogen donors raises a subsidiary question concerning the mechanism outlined in Scheme III. Though anthraquinone may arise from the cleavage of hydroperoxides **22** (e.g., **2a**[13]), derived from radicals **15**, which are known to be very prone to such a cleavage, in particular when traces of acids are present, a more satisfactory explanation can be suggested (see Scheme V). It is possible that radicals $R^1O\cdot$ and **15** coming from the fragmentation of **14** undergo, at least in part, a cage recombination to the transient trioxide **23**. Then the latter would be able to cleave by two competing ways: either along path a to give back the initial radicals or along path b to give the alkoxy radical **24**, which would lead easily to **10** by homolytic β-scission. Isolation of small fractions of 10-hydroxy-10-methyl-9-anthrone (**12**) in several assays may be also in keeping with the assumed formation of radical **24** ($R^2 = CH_3$). The fact that intermediate trioxides **23** have not been detected by NMR is not surprising since their instability is presumably comparable to that of ozonides **7** (see ref 4).

Regarding now the first step of the decomposition, it is interesting to note that the various identified products may be considered in all cases but one as deriving from diradical **14**. The only exception arises with the ozonide bearing a phenyl substituent (**7k**), as in the series of ozonides **1**. The alternate pathway in that case may be explained by a migration of the phenyl substituent to oxygen in diradical **17** followed by the fragmentation of **18** into O_2 and diether **13k**. This apparent regiospecificity may result from a high selectivity of the cleavage of the peroxide bond [O(1)–O(2)] close to the alkoxy substituent in ozonides **7** or possibly from the subsequent kinetic behavior of diradicals **14** and **17** in equilibrium through **7**. In diradical **14** a very fast scission to **15** is indeed expected, whereas in **17** a competing process could occur only when R^2 is a phenyl radical owing to the high migratory aptitude of this group.

A further point relevant to these decompositions comes from the electronic state of the released oxygen. It is well-known that a number of classes of compounds, such as phosphites, react with ozone to form unstable ozone–substrate adducts able to give off singlet oxygen by thermal decomposition.[6] In the present case, it seems that oxygen is produced essentially in the triplet state, since after decomposition of ozonide **7e** in the presence of singlet oxygen traps, such as cyclohexene or 1,2-dimethylcyclohexene, no characteristic oxidation derivatives of these compounds could be detected.

Experimental Section

NMR spectra have been recorded on a Varian A.60 spectrometer ($\delta_{Me_4Si} = 0$). Separation procedures were made by TLC on silica gel Merck GF 254 (e = 1 mm). Instantaneous melting or decomposition points were measured on Maquenne or Köfler blocks.

9-Alkoxyanthracenes. 9-Alkoxyanthracenes **6**, which were all known except **6g,h**, have been prepared according to the

(6) See Murray, R. W. "Singlet Oxygen"; Wasserman, H. H. Murray, R. W., Eds.; Academic Press: New York, 1979; p 106.

original literature by alkylation of the corresponding anthrones[7,8] or from 9,10-diacetoxyanthracene in case of **6j**.[9] Their characteristic ^1H NMR data are given in Table IV.

Synthesis of 9-(Isopropyloxy)-10-methylanthracene (6g). 10-Methyl-9-anthrone (0.5 g) in 25 mL of isopropyl alcohol were heated to reflux under N_2. Then alternate additions of aqueous KOH (d = 1.33) and isopropyl bromide were made until no more color developed on addition of KOH. After water dilution and neutralization, the product was extracted by ethyl acetate. Purified by TLC on silica gel (CH_2Cl_2), **6g** is a yellow oil (0.358 g; 58%): UV (ether) λ_{max} 403 nm (log ϵ 3.85), 381 (3.91), 361 (3.71), 260 (5.10),; mass spectrum (70 eV, 100 °C), m/e (relative intensity) 250 (10), 209 (26), 208 (100), 207 (44), 178 (36). Anal. Calcd for $C_{18}H_{18}O$: C 86.36; H, 7.25 (M = 250). Found: C, 86.16; H, 7.33. (^1H NMR in Table IV.)

Synthesis of 9-(Benzyloxy)-10-methylanthracene (6h). 10-Methyl-9-anthrone (0.3 g), 1.08 g of Na_2CO_3, and 1.5 mL of benzyl chloride were refluxed in 5 mL of dimethylformamide under N_2 until discoloration. After dilution with ethyl acetate and filtration, the solution was washed with water up to neutrality and the solvent removed. After TLC on silica gel (C_6H_6) and recrystallization (CH_3OH), the product appears as pale yellow crystals: mp 107–108 °C (0.238 g; 66 %); UV (ether) λ_{max} 402 nm (log ϵ) 3.72), 380 (3.75), 360 (3.55), 344 (3.25), 260 (4.70), 252 (4.75); mass spectrum (70 eV, 150 °C), m/e (relative intensity) 298 (60), 296 (36), 208 (29), 207 (100), 206 (37), 178 (33), 91 (79), 89 (31), 76 (33), 65 (27). Anal. Calcd for $C_{22}H_{18}O$: C, 88.56; H, 6.08 (M = 298). Found: C, 88.47; H, 6.15. (^1H NMR in Table IV.)

General Procedure for Ozonolysis. An ozone–oxygen stream (O_3/O_2, 5 %) was bubbled through a solution of 0.1 g of 9-alkoxyanthracene (**6**) in methanol (4 mL) at −78 °C until the greenish fluorescence of the starting material disappeared (~15 min). After excess ozone was swept with nitrogen at the same temperature, the crystalline ozonide **7** was quickly collected by centrifugation in small conic tubes, washed with methanol, and dried under vacuum at 0 °C for 15–30 min. Yields are given in Table I. In the solid state, ozonides **7** explode when projected on the Köfler block but are stable for several hours around 0 °C.

Isolation of the Decomposition Products. The ozonides **7** (0.05 g) were immediately redissolved in CD_2Cl_2 (1 mL) cooled to −60 °C. The solutions were allowed to return slowly to ambient temperature, and the decompositions were either followed by ^1H NMR or the resulting products were separated by TLC on silica gel (CH_2Cl_2). In the latter case the isolated products may not reflect exactly the initial distribution as some degradation may occur, in particular with hydroperoxide **2a**. Moreover slight variations are observed, according to the rate of warm-up.

The eluted products were the following.

From ozonide 7e: anthraquinone (**10**) (8 mg, 21%); 10-methoxy-10-methyl-9-anthrone (**8e**) (22 mg, 50%); 10,10′-dimethylbi-9-anthrone (**9**) (6 mg, 16%). Minor amounts of 10-hydroperoxy-10-methyl-9-anthrone (**2a**) and of 10-hydroxy-10-methyl-9-anthrone (**12**) have been also isolated in several assays. **8e**: mp 115–116 °C;[3b,11] ^1H NMR (CD_2Cl_2) δ 1.69 (s, 3 H, CH_3), 2.88 (s, 3H, OCH_3), 7.40–8.00 (m, 6 H, Ar), 8.25–8.50 (m, 2 H, H_1, H_8); IR (KBr) 1665 cm^{-1}. **9**: mp 283–284 °C;[3b] ^1H NMR (CD_2Cl_2) δ 1.28 (s, 6 H, CH_3), 7.00–8.40 (m, 16 H, Ar).

From ozonide 7f: **10** (5 mg, 14%); **9** (4 mg, 10%); 10-ethoxy-10-methyl-9-anthrone (**8f**) (20 mg, 45%); 10-methyl-9-anthrone (**11**) (5 mg, 14%). **8f**: oil, ^1H NMR (CD_2Cl_2) δ 1.11 (t, 3 H, J = 7 Hz, CH_3), 1.70 (s, 3 H, CH_3), 3.01 (q, 2 H, J = 7 Hz, CH_2), 7.40–8.05 (m, 6 H, Ar), 8.25–8.45 (m, 2 H, H_1, H_8); IR (KBr) 1670 cm^{-1}; mass spectrum, m/e (relative intensity) 252 (8), 237 (14), 207 (100), 206 (59), 178 (47), 152 (13). Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39 (M = 252). Found: C, 80.70; H, 6.43. **11**: mp 64–65 °C;[12] ^1H NMR (CD_2Cl_2) δ 1.56 (d, 3 H, J = 7 Hz, CH_3), 4.28 (q, 1 H, J = 7 Hz, H_{10}).

From ozonide 7g: **10** (5 mg, 14%); **9** (12 mg, 34%); 2-acetyl-2′-hydroxybenzophenone, mp 105 °C (3 mg, 8%), identified with an authentic sample;[3b,13] 10-hydroperoxy-10-methyl-9-anthrone (**2a**)[3b] (6 mg, 15%); 10-hydroxy-10-methyl-9-anthrone (**12**) (4 mg, 10%). **2a**: mp 159 °C[3a,b] dec; ^1H NMR (CD_2Cl_2) δ 1.68 (s, 3 H, CH_3), 7.37–8.07 (m, 6 H, Ar), 8.19–8.39 (m, 2 H, H_1, H_8), 8.46 (s, 1 H, exchanged in D_2O). **12**: mp 154 °C, identified with an authentic sample;[12] ^1H NMR (CD_2Cl_2) δ 1.64 (s, 3 H).

From ozonide 7h (from a solution of 0.1 g of **6h** ozonized at −78 °C): **10** (26 mg, 38%); **9** (9 mg, 13%); **2a** (17 mg, 21%).

From ozonide 7i (from a solution of 0.1 g of **6i** ozonized at −78 °C): **10** (41 mg, 41%); **8i** (46 mg, 43%), identified with an authentic sample.[14] **8i**: mp 100–101 °C;[7a] ^1H NMR (CD_2Cl_2) δ 2.98 (s, 3 H, CH_3), 5.86 (s, 1 H, H_{10}), 7.40–8.00 (m, 6 H, Ar), 8.30–8.50 (m, 2 H, H_1, H_8); IR (KBr) 1670 cm^{-1}.

From ozonide 7j: **10** (6 mg, 17%); **8j** (32 mg, 72%), identified with an authentic sample. **8j**: mp 128 °C;[9] ^1H NMR (CD_2Cl_2) δ 2.94 (s, 6 H, CH_3), 7.40–8.00 (m, 6 H, Ar), 8.30–8.50 (m, 2 H, H_1, H_8); IR (KBr) 1670 cm^{-1}.

From ozonide 7k: **13k** (6 mg, 13%), whose structure was deduced from spectral data; **8k** (33 mg, 73%), identified with an authentic sample;[15] **10** (3 mg, 10%). **13k**: yellow crystals, mp 99–100 °C; UV (ether) λ_{max} 401 nm (log ϵ 3.83), 379 (3.86), 360 (3.65), 342 (3.37); mass spectrum (70 eV, 100 °C), m/e (relative intensity) 301 (19), 300 (86), 286 (21), 285 (100), 257 (30), 152 (29), 77 (57), 51 (26); ^1H NMR (CD_2Cl_2) δ 4.17 (s, 3 H, OCH_3), 6.65–7.60 (m, 9 H, Ar), 7.90–8.25 (m, 4 H, Ar). Anal. Calcd for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37 (M = 300). Found: C, 84.13; H, 5.58. **8k**: mp 169–170 °C;[15] ^1H NMR (CD_2Cl_2) δ 3.05 (s, 3 H, OCH_3), 7.20–7.75 (m, 11 H, Ar), 8.35–8.55 (m, 2 H, H_1, H_8); IR (KBr) 1670 cm^{-1}.

Decomposition of 7e in the Presence of Added H Donors. With CD_3OD. Crystalline ozonide **7e** (60 mg) was dissolved in CD_2Cl_2 (1 mL) at −60 °C, and 0.1 mL of CD_3OD was added. Decomposition occurred when the solution was brought back to ambient temperature. The solvent was evaporated at room temperature, and the residual oil was separated by TLC on silica gel (CH_2Cl_2) to give the following in order of elution: **10** (2.5 mg, 5%); **8′e** (34 mg, 64%); **9** (1 mg, 2%); **2a** (2.5 mg, 5%), **12** (4.5 mg, 9%).

With C_2H_5OH. The same procedure as above run on 79 mg of crystalline ozonide **7e** in CD_2Cl_2 (1 mL) to which was added 0.1 mL of ethanol led to the following: **10** (7 mg, 12%); **8f** (55 mg, 74%); **2a** (2 mg, 3%); **12** (4 mg, 6%).

With $(CH_3)_2CHOH$. The same procedure as above run on 50 mg of crystalline ozonide **7e** in CD_2Cl_2 (1 mL) to which was added 0.1 mL of 2-propanol led to the following: **10** (14.5 mg, 38%); **8e** (8 mg, 18%); **9** (7 mg, 18%); **2a** (7 mg, 15%).

With 2,4,6-Tri-*tert*-butylphenol (19). In Equimolar Proportion. To 62 mg (0.23×10^{-3} mol) of crystalline ozonide **7e** dissolved at −60 °C in 1 mL of CH_2Cl_2 was added a solution of 60 mg (0.2×10^{-3} mol) of **19** in 1 mL of CH_2Cl_2 cooled to −60 °C. As the temperature was raised to around −30 °C, a bluish color appeared while the gas evolution took place. On going to ambient temperature the solution turned pale yellow. After evaporation of the solvent, the separation by TLC on silica gel (CH_2Cl_2) gave the following: **19** (37 mg, 62%); **20** (30 mg, 26%); **8e** (22 mg, 40%); **2a** (7 mg, 13%).

In Excess. The same procedure was applied to 100 mg (0.4×10^{-3} mol) of crystalline ozonide **7e** in 1 mL of CH_2Cl_2 to which was added 400 mg (1.6×10^{-3}) of **19** in 1 mL of CH_2Cl_2 at −60 °C. Separation by TLC afforded the following: **19** (312 mg, 78%); **21** (28 mg, 3%); **20** (76 mg, 41%); **8e** (24 mg, 27%); **2a** (22 mg, 25%). **21**, mp 147–178 °C was identified with an authentic sample prepared according to ref[16]: ^1H NMR (CD_2Cl_2) δ 0.80 (s, 9 H, *t*-Bu-4), 1.27 (s, 18 H, *t*-Bu-2, *t*-Bu-6), 6.63 (s, 2 H, H_3, H_5). **20**: mp 120–121 °C; ^1H NMR (CD_2Cl_2) δ 0.48 (s, 9 H, *t*-Bu-4), 1.32 (s, 18 H, *t*-Bu-2′, *t*-Bu-6′), 1.53 (s, 3 H, CH_3-9), 6.47 (s, 2 H, H_3, H_5), 7.20–7.80 (m, 6 H, Ar), 8.20–8.40 (m, 2 H, Ar); IR (KBr) 1610 (C=C), 1650 and 1670 cm^{-1} (C=O); mass spectrum (70 eV, 100

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°C), m/e (relative intensity) 262 (7), 247 (4), 220 (20), 209 (87), 208 (67), 207 (51), 180 (49), 177 (49), 152 (80), 76 (43), 57 (67), 41 (100). Anal. Calcd for $C_{33}H_{40}O_4$: C, 79.16; H, 8.05 (M = 500). Found: C, 79.06; H, 8.19.

In accordance with its structure, pyrolysis of **20** (10 mg) at 200 °C during 2 min gave a mixture whose constituents, separated by TLC on silica gel (CH_2Cl_2), were as follows: 2,6-di-*tert*-butylbenzoquinone[17] (3 mg, 20%); **10** (2 mg, 40%); **12** (2 mg, 45%).

With Hydroquinone (HQ). In CD_2Cl_2–CD_3OD. To 60 mg (0.22×10^{-3} mol) of crystalline ozonide **7e** in 1 mL of CD_2Cl_2 at −60 °C was added 48 mg (0.44×10^{-3} mol) of hydroquinone dissolved in 1 mL of CD_3OD cooled to −60 °C. The residue obtained after reaction and evaporation of the solvents was extracted with CH_2Cl_2. Insoluble black crystals of quinhydrone (QH) (23 mg, 24%), mp 171 °C, were isolated, and separation by TLC of the soluble fraction gave the following: **10** (3.2 mg, 7%); **8e** (12 mg, 23%); **9** (4 mg, 9%); **12** (24 mg, 48%).

The possible reduction of hydroperoxide **2a** by QH was checked as follows: To 15 mg of **2a** in 1 mL of CH_2Cl_2 was added a solution of 20 mg of QH in 1 mL of CH_3OH; usual separation afforded **12** (12 mg, 82%).

In CH_2Cl_2–CH_3CN. To 64 mg (0.24×10^{-3} mol) of crystalline ozonide **7e** in 1 mL of CH_2Cl_2 at −60 °C was added 53 mg (0.48×10^{-3} mol) of hydroquinone in 1 mL of acetonitrile cooled to 60 °C. As the temperature was raised to ambient, black crystals of quinhydrone (QH) precipitated out and were filtered (42 mg, 40%). Usual separation led to the following: **10** (2 mg, 4%); *p*-benzoquinone, mp 116 °C (3.6 mg, 7%); **2a** (47 mg, 82%).

Decomposition of ozonide **7e** in the mixture CH_2Cl_2–CH_3CN without added HQ led to the results given in Table III.

Decomposition of Ozonide 7e in the Presence of $^1O_2$ Traps. The principle of the method reported in the case of 1-phospha-2,8,9-trioxaadamantane[18] has been followed.

For example, to a solution of 60 mg (0.22×10^{-3} mol) of crystalline ozonide **7e** in 1 mL of CD_2Cl_2 at −70 °C was added 30 μL of 1,2-dimethylcyclohexene, and the ^1H NMR spectrum of the mixture was recorded. After return to ambient temperature, the ^1H NMR spectrum showed no traces of the olefinic hydroperoxides derived from 1,4-dimethylcyclohexene. Further separation led to the following: **10** (5 mg 10%); **8e** (18 mg, 34%); **9** (14 mg, 30%); **2a** (6 mg, 11%); **12** (1 mg, 2%).

The same procedure applied to 80 mg (0.3×10^{-3} mol) of ozonide **7e** and 30 μL (0.3×10^{-3} mol) of cyclohexene led to an identical finding, and separation gave the following: **10** (5 mg, 8%); **8e** (25 mg, 35%); **9** (16 mg, 26%); **2a** (19 mg, 27%); **12** (6 mg, 9%). The increase noted on the yields of **2a** and **12** seems to result from the H-donor ability of cyclohexene.

Registry No. **2a**, 17526-22-6; **6e**, 21992-33-6; **6f**, 24165-83-1; **6g**, 98612-70-5; **6h**, 98612-71-6; **6i**, 2395-96-2; **6j**, 2395-97-3; **6k**, 17803-79-1; **7e**, 98612-72-7; **7f**, 98612-73-8; **7g**, 98612-74-9; **7h**, 98612-75-0; **7i**, 98612-76-1; **7j**, 71955-40-3; **7k**, 98612-77-2; **8e**, 17104-31-3; **8f**, 98612-79-4; **8i**, 14629-83-5; **8j**, 40628-58-8; **8k**, 25548-89-4; **9**, 98612-78-3; **10**, 84-65-1; **12**, 17104-31-3; **13k**, 98612-80-7; **19**, 732-26-3; **20**, 98612-81-8; **21**, 1975-14-0; HQ, 123-31-9; 1,2-dimethylcyclohexene, 1674-10-8; cyclohexene, 110-83-8; 10-methyl-9-anthrone, 73653-01-7; 2-acetyl-2′-hydroxybenzophenone, 17526-21-5; 2,6-di-*tert*-butylbenzoquinone, 719-22-2.

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Biomimetic Studies Using Artificial Systems. 3.[1,2] Design, Synthesis, and Inclusion Complex Forming Ability of a Novel Water-Soluble Paracyclophane Possessing Diphenylmethane Skeletons[3]

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A novel water-soluble paracyclophane, CP44 (1), was designed and synthesized as a host molecule possessing a hydrophobic cavity to capture organic guests in water. X-ray crystallographic study revealed the formation of a 1:1 *inclusion* complex, and not a simple stacked complex, between protonated CP44 and durene. This is the first *direct* evidence showing the ability of a water-soluble cyclophane to form an inclusion complex. The inclusion of hydrophobic guests *in water* (acidic condition) was also evidently observed by several kinds of spectra (^1H and ^{13}C NMR, fluorescence).

From the viewpoint of synthetic organic chemistry, the most significant aspects of biological reactions—such as those between enzymes and substrates—are their extremely high speed and selectivity that originate from the prior formation of specific molecular complexes, i.e., *host–guest complexes*.[4,5] These complexes are characteristic in that they are stoichiometric inclusion complexes formed by macromolecular biological hosts, e.g., enzymes, antibodies, and receptors. In such complexes the guest (substrate) is strongly captured and tightly fixed in the inclusion cavity of its specific host, resulting in the formation of a highly structured molecular complex. The highly structured nature of the complex is essential to effect high speed and selectivity in the intracomplex chemical conversion, which is the step subsequent to the guest inclusion (eq 1). If the style of such biological

$$H + G \rightleftharpoons H{\cdot}G \rightarrow H{\cdot}P \rightarrow H + P \qquad (1)$$

H = host, G = guest (substrate), P = product

reactions could be mimicked with simpler organic systems,

(1) This paper is dedicated to Professor Shun-ichi Yamada on the occasion of his 70th birthday.

(2) Part 2 of this series: Sasaki, S.; Kawasaki, M.; Koga, K. *Chem. Pharm. Bull.* **1985**, *33*, 4247-4266.

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