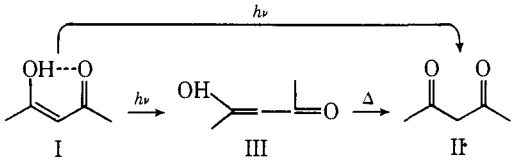
diketones II_{a-e}, II_h could not be followed by means of the flash technique. We therefore could not distinguish between the two possible modes of formation of II, i.e., directly or via III. The



effect of oxygen favors the direct path: In oxygen-flushed solutions the relative quantum yield of photoketonization I → II is double that in nitrogen-flushed solutions, while the reverse holds for the photoisomerization I → III. One possibility is that photoketonization takes place in the singlet state, while photoisomerization involves intersystem crossing, which may be expected to be very efficient. In this respect photoketonization would resemble the well-known 1,3 migration which characterizes enolic systems.[4] Another possible explanation would be that both II and III arise from a common intermediate by competitive decays, one of which is enhanced by oxygen at the expense of the other.

Finally, the present results indicate the usefulness of photo-induced relaxation methods in studies of the three processes III → I, II → I, III → II, including proton-transfer reactions in nonpolar solvents.[3]

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Prostanoid Endoperoxide Model Compounds: 1-Oxatrimethylene Diradicals in the Thermolysis and Photolysis of 1,2-Dioxolanes[1]

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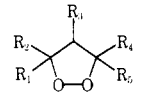
Abstract: Thermo- and photodeketonization of a series of methyl and phenyl substituted 1,2-dioxolanes, considered as prostanoid endoperoxide model compounds, affords fragmentation and rearrangement ketones and epoxides as the major volatile products. The product data show that the relative leaving group abilities for deketonization are in the order $Ph_2C{=}O$ > MePhC=O > $Me_2C{=}O$. Furthermore, with increasing leaving group ability, or with increasing phenylation of the dioxolane, the efficiency for the rearrangement increases, but the efficiency for cyclization decreases. In the rearrangement methyl outweighs phenyl migration and the ratio of methyl to phenyl shift increases with increasing leaving group ability. Kinetics of the thermolysis of the tetramethyl- and tetraphenyl-1,2-dioxolanes gave $\Delta H^{\ddagger}$ = 27.0 ± 0.3 and 21.7 ± 1.0 kcal/mol and $\Delta S^{\ddagger}$ = −24.8 ± 2.0 and −30.8 ± 2.2 gibbs/mol, respectively, revealing that these activation parameters are a function of leaving group structure. Finally, a stereolabeling experiment on (*S*)-(−)-3,3,4-trimethyl-1,2-dioxaspiro[4.4]nonane shows that the rearrangement ketone (*S*)-(−)-2-methylcyclohexanone is formed with 8.4 ± 2.0% net retention of configuration, under conditions where the rearrangement ketone is optically stable. On the basis of these product, kinetic, and stereolabeling results the thermo- and photodeketonization of 1,2-dioxolanes is postulated to proceed via a 1-oxatrimethylene diradical.

The involvement of endoperoxides **1** as precursors to prostaglandins and the recent demonstration[3] that such prostanoid endoperoxides show even greater physiological activity than the prostaglandins themselves have served as main impetus in the elucidation of these novel cyclic peroxides. Although the syntheses of authentic endoperoxides **1** have not been reported,[4] the simpler 1,2-dioxolanes **2**, which can be considered as model compounds, have been known for several decades.[5] Recently several new synthetic methods for 1,2-dioxolanes have been described, e.g., perhydrolysis of 1,3-disulfonates,[6]

Table I. Properties of 1,2-Dioxolanes 2

	 R_1 R_2 R_3 R_4 R_5	Method	Yield, %	Physical constants: Bp, °C (mm), or mp, °C	Physical constants: $n^{20}D$	Isotropic distr *m/e*, %: Calcd	Isotropic distr *m/e*, %: Exptl	NMR[a] (CCl_4), ppm (Me_4Si)
2a	Me Me H Me Me	A[b]	31	Bp 46–47 (25)	1.4080[c]	100.0 8.0 0.7	100.0 7.8 0.7	—
2b	Me Me H Me Ph	A[b]	76[d]	Bp 48–52 (0.03)	1.5046	100.0 13.3 1.2	100.0 13.4 1.3	1.15 (3, s) 1.44 (3, s) 1.60 (3, s) 2.62 (2, AB q, J = 7 Hz) 7.35 (5, m)
2c	Me Ph H Me Ph	B[e]	50[d]		1.5514	100.0 18.8 2.2	100.0 19.0 2.3	1.40 (3, s) 1.65 (3, s) 2.90 (2, AB q, J = 7 Hz) 3.05 (3, s) 7.20 (10, m)
2d	Me Ph H Ph Ph	B[e]	45	Mp 91–92		100.0 24.2 3.3	100.0 25.0	1.50 (3, s) 3.45 (2, s) 7.10 (15, m)
2e	Ph Ph H Ph Ph	C[f]	46	Mp 178–179		*g*		4.00 (2, s) 7.32 (20, m)

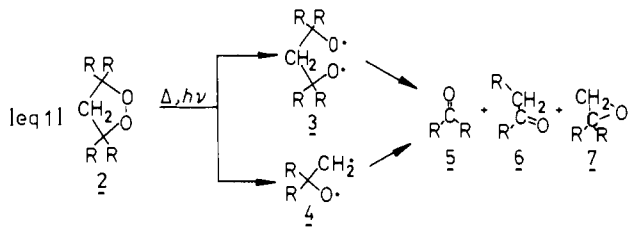
[a] The order followed is no. of H, multiplicity, coupling constant. [b] Diol, 98% H_2O_2 (*caution!*). [c] Lit.[5] bp 46 °C (25 mm), $n^{20}D$ 1.4080. [d] Purified by column chromatography on silica gel. [e] Diol, 50% H_2O_2 and H_2SO_4 (*caution!*). [f] Diol, 98% H_2O_2 (*caution!*), tosic acid. [g] Satisfactory elemental analysis.

reaction of 1,3-dibromides with superoxide ion,[7] and singlet oxygenation of cyclopropanes.[8] Yet no detailed mechanistic study of the thermolysis and photolysis of these five-membered ring cyclic peroxides has been reported. Such information should be relevant in the behavior of prostanoid endoperoxides.

1

2

In analogy to previous mechanistic work on β-peroxylactones,[9] 4-alkylidene-1,2-dioxolanes,[10] 4-aza-1,2-dioxolanes,[11] *N*-nitroso-4-aza-1,2-dioxolanes,[12] and ozonides,[13] we anticipated that either the 1,5-dioxapentamethylene diradicals **3** or the 1-oxatrimethylene diradicals **4** would intervene as precursors to the fragmentation ketones **5,** rearrangement ketones **6,** and epoxides **7** (eq 1), depending on whether deketonation of the 1,2-dioxolanes **1** takes place stepwise or synchronously. We now present a detailed account[14] of the mechanism of thermolysis and photolysis of 1,2-dioxolanes **1,** providing evidence for the intervention of the 1-oxatrimethylene diradical **4.**



Experimental Section

Boiling points and melting points are uncorrected. The latter were taken on a Thomas-Hoover melting point apparatus. All new compounds had satisfactory elemental analyses, which were performed by Alfred Bernhardt (D-S251 Elbach über Engelskirchen, West Germany). Infrared spectra were made on a Perkin-Elmer Infracord 237B. ^1H NMR spectra were taken on a Varian T-60 and the optical rotations were measured on Perkin-Elmer Model 141 polarimeter. The mass spectra were taken on a Hitachi Perkin-Elmer Model RMS-4 spectrometer and GLC analyses were performed on a Varian 202-B Aerograph.

Syntheses. All commercially available solvents, starting materials, and authentic samples for product comparison and control experiments were rigorously purified according to reported procedures. The remaining compounds required in this research, except those given below, were prepared and purified according to literature methods and will not be described here.[17]

(*S*)-(+)-3,3,4-Trimethyl-1,2-dioxaspiro[4.4]nonane (2f). A 100-mL, one-necked round-bottom flask, provided with a magnetic spin bar, was charged with 1.0 g (5.8 mmol) of (*S*)-(−)-3-(1-hydroxycyclopentyl)-2-methylbutan-2-ol (**8**) in 10 mL of ether. The solution was cooled to 0–5 °C by means of an ice bath and while stirring magnetically 25 mg of tosic acid catalyst was added. By remote control behind a safety shield were added dropwise, while stirring and cooling efficiently, 3 mL of 98% H_2O_2 (*Caution!*), using a Cheng tube.[15,18] After completion of H_2O_2 addition (ca. 15 min), the reaction mixture was allowed to warm up to room temperature (ca. 28 °C) and stirred for an additional 9 h. The reaction mixture was worked up by adding three volumes of ice water, transferred to a separatory funnel, extracted with 3 × 50 mL of CH_2Cl_2, washed with 3 × 25 mL of saturated aqueous $(NH_4)_2SO_4$ and 1 × 25 mL of water, and dried over anhydrous $MgSO_4$. Rotoevaporation (ca. 30 °C, 25 mm) of the solvent and fractional distillation afforded a 48% yield of the pure 1,2-dioxolane **2f:** bp 57–58 °C (0.9 mm); $n^{20}D$ 1.4560; α^{20}_{589} +1.57°, α^{20}_{578} +1.62°, α^{20}_{546} +1.88°, α^{20}_{436} +3.73°, and α^{20}_{365} +8.28° (*c* 6.11, CCl_4). The 1,2-dioxolane structure is based on $LiAlH_4$ reduction to the corresponding 1,3-diol **8** in 94% yield, mp 87–88 °C, mmp 87–88 °C, α^{20}_{589} −22.4 (*c* 1.82, CCl_4), and the following spectral data: IR (CCl_4) 2955, 2875, and 1475 (aliphatic CH), 1380 and 1365 (*gem*-dimethyl), 1185 (C-O), and 950 cm^{-1} (alkyl peroxide); NMR (60 MHz) δ (CCl_4, Me_4Si) 0.96 (3 H, d, J = 7 Hz, CH_3CH), 1.12 (3 H, s, CH_3), 1.22 (3 H, s, CH_3), 1.60 (8 H, m, $(CH_2)_4C$), and 2.35 (1 H, q, J = 7 Hz, $CHCH_3$); mass spectrum (70 eV) *m/e* (rel intensity) 43 (100), 170 (40, P), 171 (4.5, P + 1), and 172 (0.5, P + 2).

The remaining 1,2-dioxolanes were prepared analogously with only minor alterations. The results are summarized in Table I. As chemical structure proof, the 1,2-dioxolanes were hydrogenated catalytically[16] over platinum catalyst or reduced with $LiAlH_4$ to the respective 1,3-diols; the latter were purified by fractional recrystallization and their structure confirmed spectrally and by mixture melting point with authentic materials.[17]

(*S*)-(−)-3-(1-Hydroxycyclopentyl)-2-methylbutan-2-ol (8). Method A. The 1,3-diol **8** was prepared in 50% yield analogous to Meerwein's method:[19] mp 87–88 °C; α^{20}_{589} −20.86°, α^{20}_{578} −21.71°, α^{20}_{546} −26.6°, α^{20}_{436} −41.20°, and α^{20}_{265} −63.60° (*c* 10.66, CCl_4) and α^{20}_{589} −22.2° (*c* 1.82, CCl_4), by the addition of excess methylmagnesium bromide to methyl (*R*)-(+)-2-(1-hydroxycyclopentyl)propionate (**15**) in ether. The spectral data follow: IR (CCl_4) 3300 (asso-

ciated OH), 2930 (aliphatic CH), 1385 and 1370 (*gem*-dimethyl), 1100 (C-O), and 950 cm^{-1} (alkyl peroxide); NMR (60 MHz) δ (CCl_4, Me_4Si) 0.82 (3 H, d, J = 7 Hz, CH_3CH), 1.20 (6 H, s, $(CH_3)_2C$), 1.65 (9 H, m, $(CH_2)_4C$ and $CHCH_3$), and 5.42 (2 H, s, OH).

Method B. The 1,3-diol **8** was prepared in 55% yield analogous to the method of Franke and Kolin:[20] mp 86-87 °C; α^{20}_{589} −27.2°, α^{20}_{578} −23.1°, α^{20}_{546} −26.3°, α^{20}_{436} −44.3°, and α^{20}_{365} −68.8° (*c* 9.77, CCl_4), by the addition of excess methylmagnesium bromide to (*R*)-(−)-3-(hydroxycyclopentyl)-2-butanone (**9**) in ether.

Methyl (*R*)-(−)-2-(1-hydroxycyclopentyl)propionate (15) was prepared in 99% yield, bp 48-48.5 °C (0.05 mm), n^{20}_D 1.4564, α^{20}_{589} +12.2°, α^{20}_{578} +12.8°, α^{20}_{546} +14.7°, α^{20}_{436} +24.9°, and α^{20}_{365} +42.2° (*c* 10.42, CCl_4), by esterification of (*R*)-(+)-2-(1-hydroxycyclopentyl)propionic acid (**16**) with 250 mL of ethereal diazomethane solution (10 mg/mL).[21] The spectral data follow: IR (CCl_4) 3510 (free OH), 2995 (aliphatic CH), 1720 (ester C=O), 1445 and 1428 (aliphatic CH), and 1105 cm^{-1} (C-O); NMR (60 MHz) δ (CCl_4, Me_4Si) 1.22 (3 H, d, J = 6 Hz, CH_3CH), 1.60 (8 H, m, $(CH_2)_4C$), 2.48 (1 H, q, J = 6 Hz, $CHCH_3$), 3.65 (3 H, s, CH_3O), and 3.82 (1 H, s, OH).

2-(1-Hydroxycyclopentyl)propionic acid (16) was prepared in 63% yield analogous to the method of Adam, Baeza, and Liu,[22] mp 58-59 °C (lit.[23] mp 59 °C), by condensing the lithium α-lithiopropionate with cyclopentanone in THF. The racemic β-hydroxy acid was resolved by combining a hot solution of 20.4 g (0.129 mol) of the acid **16** in 50 mL of absolute ethanol with a hot solution of 42.2 g (0.13 mol) of quinine in 300 mL of absolute ethanol and allowed to stand overnight. The profuse precipitate was collected on a Büchner funnel and dried at reduced pressure (ca. 35 °C, 10 mm), affording 30.0 g (50%) of crude quinine salt, mp 165-173 °C. This salt was recrystallized from ether-ethanol (1:3) until constant melting point (ca. ten times) to give 23 g (38%) of quinine salt, mp 176-176.5 °C. The free β-hydroxy acid was recovered by treating an 800 mL CH_2Cl_2 suspension of the quinine salt with 10% aqueous HCl. The CH_2Cl_2 layer was washed with 3 × 250 mL of 10% aqueous HCl and with 2 × 100 mL of H_2O and dried over $MgSO_4$. Rotoevaporation of the solvent (ca. 28 °C, 30 mm) gave 7.2 g (35%) of crude β-hydroxy acid **16,** mp 50-56 °C. The pure acid was obtained by two recrystallizations from ether-hexane (1:10): 6.5 g (31.8%, based on racemic acid), mp 62-62.5 °C, α^{20}_{589} +3.75°, α^{20}_{578} +3.95°, α^{20}_{546} +4.50°, α^{20}_{436} +7.71°, and α^{20}_{365} −11.8° (*c* 12.53, CCl_4). The spectral data follow: IR (CCl_4) 3500-2600 (associated OH), 2950 and 2875 (aliphatic CH), 1700 (acid C=O), and 1450 and 1375 cm^{-1} (aliphatic CH); NMR (60 MHz) δ (CCl_4, Me_4Si) 1.22 (3 H, d, J = 7 Hz, CH_3CH), 1.60 (8 H, s, $(CH_2)_4C$), 1.45 (1 H, q, J = 7 Hz, $CHCH_3$), and 7.15 (2 H, s, OH).

(*R*)-(−)-3-(1-Hydroxycyclopentyl)-2-butanone (9) was prepared in 34% yield analogous to Seebach's method,[24] bp 77-78 °C (1.3 mm), n^{23}_D 1.4608, α^{25}_{589} −24.4°, α^{25}_{578} −25.8°, α^{25}_{546} −30.3°, α^{25}_{436} −64.1, and α^{25}_{365} −148.7° (*c* 4.64, CCl_4), by oxidative desulfurization of (*R*)-(+)-1-(1-hydroxycyclopentyl)-1-(2-methyl-1,3-dithianyl)-ethane (**10**) with $HgCl_2$-HgO in 75% aqueous methanol.

The spectral data follow: IR (CCl_4) 3525 (free OH), 2975 and 2875 (aliphatic CH), 1710 (ketone C=O), 1455 (aliphatic CH), 1380 (CH_3), and 1160 cm^{-1} (C-O); NMR (60 MHz) δ (CCl_4, Me_4Si) 1.15 (3 H, d, J = 7 Hz, CH_3CH), 1.60 (8 H, s, $(CH_2)_4C$), 2.20 (3 H, s, CH_3CO), and 260 (1 H, q, J = 7 Hz, $CHCH_3$); mass spectrum (70 eV) *m/e* (rel intensity) 72 (100), 156 (82, P), 57 (11, P + 1), and 158 (1, P + 2).

(*R*)-(+)-1-(1-Hydroxycyclopentyl-1-(2-methyl-1,3-dithianyl)-ethane (10) was prepared as crude product in 100% yield analogous to the method described by Seebach,[24] n^{24}_D 1.5378, α^{25}_{589} +19.0°, α^{25}_{578} +20.1°, α^{25}_{546} +22.9°, and α^{25}_{436} +40.7° (*c* 3.57, CCl_4), by reaction of 2-lithio-2-methyl-1,3-dithiane with (*S*)-(+)-2-methyl-1-oxaspiro[2.4]heptane in THF. It was not possible to purify the product **10** by fractional distillation since at the elevated distillation temperature required decomposition occurred; however, the crude **10** showed only one spot by TLC. The spectral data of the crude product follow: IR (CCl_4) 3445 (free OH), 2950, 2900, and 2850 (aliphatic CH), 1425 (aliphatic CH), 1075 (C-O), and 910 cm^{-1} (C-S); NMR (60 MHz) δ (CCl_4, Me_4Si) 1.15 (3 H, d, J = 7 Hz, CH_3CH), 1.66 (13 H, m, $(CH_2)_4C$, CH_3CH, CH_2), and 2.80 (6 H, m, $CHCH_3$, CH_2S, and OH).

(*S*)-(+)-2-Methyl-1-oxaspiro[2.4]heptane (11) was prepared in 61% yield analogous to the procedure reported by Adam and Santiago,[9b] bp 74-75 °C (86 mm), n^{25}_D 1.4368, α^{25}_{589} +14.9°, α^{25}_{578} +15.6°, α^{25}_{546} +17.3°, α^{25}_{436} +25.8°, and α^{25}_{365} +33.4° (*c* 3.44, CCl_4), by treatment of (*R*)-(−)-1-(1-hydroxycyclopentyl)ethane 1-benzenesulfonate (**12**) with sodium hydride in THF. The spectral data follow: IR (CCl_4) 3000, 2955, and 2875 (aliphatic CH), 1450 and 1445 (alkyl bending), 1375 (methyl), and 1335, 1160, 1025, and 855 cm^{-1} (epoxide); NMR (60 MHz) δ (CCl_4, Me_4Si) 1.20 (3 H, d, J = 6 Hz, CH_3CH), 1.70 (8 H, s, $(CH_2)_4C$), and 2.80 (1 H, q, J = 6 Hz, $CHCH_3$); mass spectrum (70 eV) *m/e* (rel intensity) 84 (100), 111 (64, P − 1), 112 (83, P), 113 (22, P + 1), and 114 (10, P + 2).

(*R*)-(−)-1-(1-Hydroxycyclopentyl)ethane 1-benzenesulfonate (12) was prepared in 92% yield (crude material) analogous to the procedure reported by Adam and Santiago,[9b] n^{21}_D 1.5230, α^{25}_{589} −11.3°, α^{25}_{578} −11.8°, α^{25}_{546} −13.5°, α^{25}_{430} −23.6°, and α^{25}_{305} −38.3° (*c* 2.55, 1:1.5 CCl_4-$CHCl_3$), from (*R*)-(+)-1-(1-hydroxycyclopentyl)ethanol (**13**) and benzenesulfonyl chloride in anhydrous pyridine. The crude product could not be induced to crystallize nor could it be distilled. The spectral data follow: IR (CCl_4) 3600 (free OH), 3075 (aromatic CH), 2950 and 2875 (aliphatic CH), 1450 (alkyl), 1375 and 1190 (sulfonate ester), and 1100 cm^{-1} (C-O); NMR (60 MHz) δ (CCl_4, Me_4Si) 1.20 (3 H, d, J = 6 Hz, CH_3CH), 1.55 (8 H, s, $(CH_2)_4C$), 3.20 (1 H, s, OH), 4.50 (1 H, q, J = 6 Hz, $CHCH_3$), and 7.75 (5 H, m, C_6H_5).

(*R*)-(+)-1-(1-Hydroxycyclopentyl)ethanol (13) was prepared in 52% yield according to the method of Levene and Harris,[25] bp 84-85 °C (0.7 mm), n^{24}_D 1.4723, α^{20}_{589} +0.59°, α^{20}_{578} +0.620°, α^{20}_{546} +0.77°, α^{20}_{436} +1.95°, and α^{20}_{365} +4.29° (neat), by addition of tetramethyldimagnesium bromide to (*R*)(−)-*n*-butyl lactate in ethyl ether. The spectral data follow: IR (CCl_4) 3400-3200 (associated OH), 2960 and 2875 (aliphatic CH), 1460 (alkyl), 1375 (methyl), and 1060 cm^{-1} (C-O); NMR (60 MHz) δ (CCl_4, Me_4Si) 1.15 (3 H, d, J = 6 Hz, CH_3CH), 1.60 (8 H, s, $(CH_2)_4C$), and 3.60 (2 H, m, CH_3CHOH).

Product Studies. The qualitative and quantitative GLC analyses of the thermo- and photoproducts were carried out according to the method outlined by Adam and Rios[26] and the details will not be reproduced here.[17] The molar compositions and total product balance of the thermo- and photoproducts of the 1,2-dioxolanes **1a-f** are collected in Table II. For convenience, fragmentation, cyclization, rearrangement, leaving group ability, and migratory aptitudes are given in Table III.

Kinetics. The kinetics of the thermolysis of 1,2-dioxolanes **2a** and **2e** followed the general procedure described by us previously,[27] by monitoring the carbonyl frequencies of the ketone products in the infrared. The rate constants and activation parameters are summarized in Table IV.

Results

Product Data. As can be appreciated from Table II, a great variety of products are formed in the thermolysis as well as photolysis of the 1,2-dioxolanes, especially the unsymmetrical ones. Yet in all cases the product balance was excellent. Control experiments on authentic samples of the products revealed that they were stable under the thermolysis and photolysis conditions. Exceptions are 1,1-diphenylethylene oxide and α-methylstyrene oxide, which on thermolysis gave diphenylacetaldehyde and α-phenylpropionaldehyde, respectively. The 1,1-diphenylethylene oxide was also photolabile, leading to diphenylacetaldehyde. In view of these complications, the yields of the epoxides were diagnosed in terms of the rearranged aldehyde product.

From the normalized product data (Table III) the following conclusions emerge which are of mechanistic relevance.

1. The relative leaving group ability for deketonation is $Ph_2C{=}O > PhMeC{=}O > Me_2C{=}O$ in proportions 25:10:1, normalized with respect to acetone.

2. With increasing leaving group ability the cyclization efficiency decreases, but the rearrangement efficiency increases.

3. With increasing phenylation the cyclization efficiency decreases, but the rearrangement efficiency increases.

4. For all cases studied, methyl migration predominates over

Table II. Thermo- and Photoproduct Composition of 1,2-Dioxolanes 2

					Product composition[a]									
					Fragmentation		Cyclization		Rearrangement					
	R_1 R_2 R_3	R_4 R_5	Initial mmol used	Mode	R_1COR_2	R_4COR_5			$R_1CCH(OR_2)R_3$	$R_2CCH(OR_1)R_3$	$R_4CCH(OR_5)R_3$	$R_5CCH(OR_4)R_3$	Residue, wt %	Product balance, wt %
2a	Me Me H	Me Me	3.05	Δ^c	1.052		0.374		0.137				2	99
			3.09	$h\nu^c$	0.826		0.661		0.147				4	95
2b	Me Me H	Me Ph	0.123	$\Delta^{c,d}$	0.318	0.686	0.113	0.037	0.227		0.037	0.045	18	96
			0.241	$h\nu^{c,d}$	0.346	0.441	0.324	0.303	0.117		<0.010	0.022	15	95
2c	Me Ph H	Me Ph	0.076	Δ^d	1.03		0.122		0.102	0.282			14	99
			0.094	$h\nu^d$	0.836		0.396		0.075	0.159			18	98
2d	Me Ph H	Ph Ph	0.178	Δ^d	0.443	0.657	0.032	0.043	0.096	0.246	0.076		4	95
			0.178	$h\nu^d$	0.479	0.361	0.113	0.138	0.061	0.091	0.039		28	94
2e	Ph Ph H	Ph Ph	0.704	Δ^d	1.06		<0.010		0.775				1	96
			0.684	$h\nu^d$	0.493		0.121		0.083				34	96
2f	Me Me Me	$-(CH_2)_4-$	0.825	Δ^c	0.890	0.048			0.059		0.733		6	90
			0.858	$h\nu^c$	0.541	0.073	0.027	0.049	0.090		0.270		20	85

[a] Normalized per mole of 1,2-dioxolane decomposed. [b] All GLC analysis within 2–4% error. [c] Column: 12 ft × 0.25 in., 20% FFAP, Chromosorb P. [d] Column: 12 ft × 0.25 in., 20% SE-30 and 1% Versamid, Chromosorb P.

Table III. Relative Efficiencies of Fragmentation, Cyclization, and Rearrangement, Leaving Group Ability, and Migratory Aptitude in the Thermolysis and Photolysis of 1,2-Dioxolanes 2

			Percentage composition			Relative efficiencies				
	R_1 R_2 R_3 R_4 R_5	Mode	Frag	Cycl	Rearr	Frag	Cycl	Rearr	Leaving group ability	Migratory aptitude
2a	Me Me H Me Me		18.7 ±0.5	37.4 ±0.1	13.7 ±0.7	0.22	0.43	0.16		
2b	Me Me H Me Ph		28.7 ±0.9	15.0 ±0.5	30.9 ±0.3	0.40	0.21	0.43	0.1 ± 0.01	1.20 ± 0.06
2c	Me Ph H Me Ph	Δ^a	26.2 ±0.7	12.2 ±0.3	38.4 ±1.0	0.34	0.16	0.50		2.78 ± 0.28
2d	Me Ph H Ph Ph		29.3 ±0.7	7.5 ±0.5	41.8 ±1.5	0.35	0.09	0.52	2.54 ± 6.4	2.57 ± 0.16
2e	Ph Ph H Ph Ph		14.1 ±0.3	<1	17.5 ±0.5	0.15	0.01	0.84		
2a	Me Me H Me Me		<1.0	66.1 ±0.1	14.7 ±1.0	0.01	0.80	0.18		
2b	Me Me H Me Ph		13.1 ±0.4	62.7 ±0.3	13.9 ±0.3	0.13	0.65	0.14	0.64 ± 0.02	>220
2c	Me Ph H Me Ph	$h\nu^b$	10.3 ±0.1	39.6 ±0.1	23.4 ±0.3	0.14	0.54	0.32		2.11 ± 0.08
2d	Me Ph H Ph Ph		19.6 ±1.0	25.1 ±1.3	19.1 ±0.4	0.27	0.38	0.28	0.58 ± 0.02	1.50 ± 0.15
2e	Ph Ph H Ph Ph		9.7 ±0.6	12.1 ±0.1	8.3 ±0.2	0.25	0.31	0.21		

[a] Thermolyzed at 150–200 °C. [b] Photolyzed at 310 nm.

phenyl migration; but still more revealing, the methyl migratory aptitude increases with leaving group ability.

Stereochemical Data. The synthetic sequence for the preparation of the stereolabeled 1,2-dioxolane (*S*)-(+)-**2f**, its relative configurational correlation, and thermolysis are displayed in Scheme I. For convenience we also list the optical rotations at 589 nm for each compound. Both routes, that starting from optically pure (*R*)-(−)-*n*-butyl lactate and that involving quinine resolution of (*R*)-(+)-**16**, gave the 1,3-diol (*S*)-(−)-**8** with essentially the same optical purity. Hydrogen peroxide cyclization of the 1,3-diol (*S*)-(−)-**8** and $LiAlH_4$ reduction back to the same diol without loss of optical rotation establish the configuration and optical purity of the 1,2-dioxolane (*S*)-(+)-**2f**.

Thermolysis of a 0.94 M benzene solution of the 1,2-dioxolane (*S*)-(+)-**2f** at 165–170 °C for 17 h and collection by GLC gave (*S*)-(+)-2-methylcyclohexanone (**6f**) of 8.4 ± 2.0% optical purity, representing 8.4 ± 2% net retention or 91.6% racemization. A control experiment showed that the rearrangement ketone (*S*)-(+)-**6f** is stable under the thermolysis conditions. Authentic ketone (*S*)-(+)-**6f** of 23.3% optical purity was synthesized for this purpose by kinetic resolution of 2-methylcyclohexanone with α-pinanylborane and purified by preparative GLC. Since this experiment rules out posterior racemization of the rearrangement ketone (*S*)-(+)-**6f** under the thermolysis conditions, this product is formed 91.6% racemized in the primary step.

Kinetic Data. Within an experimental error of ca. 3% the thermolysis follows first-order kinetics. The rates are independent of solvent polarity since the rate constants are the same in benzene and acetonitrile (Table IV).

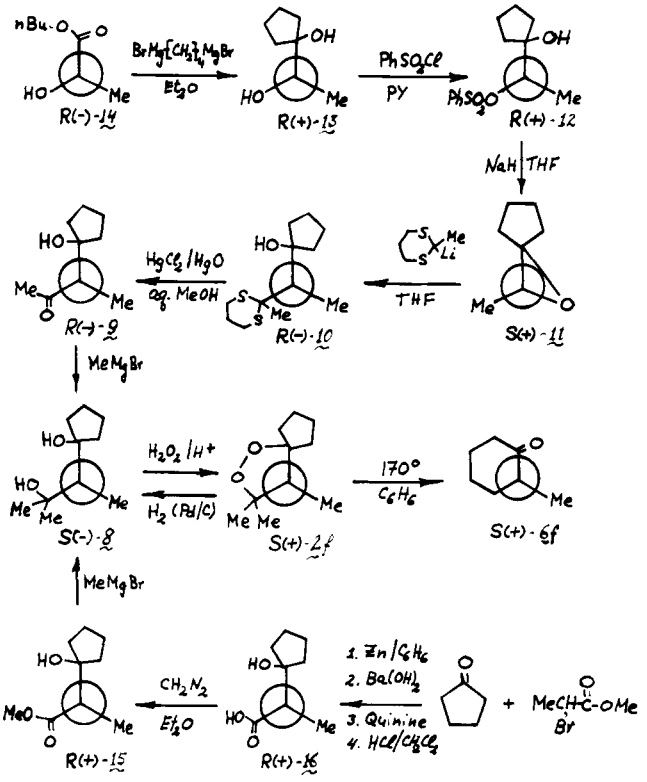
Surprising are the activation parameters as a function of methyl vs. phenyl substitution (Table IV). In both cases the activation enthalpies are unusually low and the activation entropies abnormally large and negative.[28] Furthermore, the substituent effect on $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ is well outside the experimental error, indicating that the better the leaving group, i.e., $Ph_2C{=}O > Me_2C{=}O$, the lower the $\Delta H^{\ddagger}$ and the more

Table IV. Activation Parameters and Solvent Effects in the Thermolysis of 1,2-Dioxolanes **2**

1,2-Dioxolane[a] Structure	Concn, M	Solvent	Temp,[b] K	$k \times 10^5$, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, gibbs/mol	$\Delta G^{\ddagger}$, kcal/mol
2a	0.028	C_6H_6	491.2	3.20 ± 0.15			
	0.023	C_6H_6	473.2	1.17 ± 0.06	27.0 ± 1.0	−24.0 ± 2.0	39.4 ± 1.5
	0.026	C_6H_6	463.2	0.553 ± 0.014			
	0.026	CH_3CN	491.2	4.09 ± 0.25			
2e	0.019	C_6H_6	491.2	39.0 ± 0.28			
	0.020	C_6H_6	473.2	15.3 ± 0.06	21.7 ± 1.0	−30.8 ± 2.2	37.1 ± 2.5
	0.020	C_6H_6	463.2	9.06 ± 0.05			

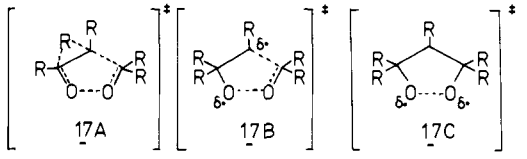
[a] Followed appearance of the carbonyl band of product ketone by infrared. [b] Temperature control within 0.05-0.10 K.

Scheme I



negative $\Delta S^{\ddagger}$ (Table IV). This structure-reactivity interplay suggests a concerted mechanism.

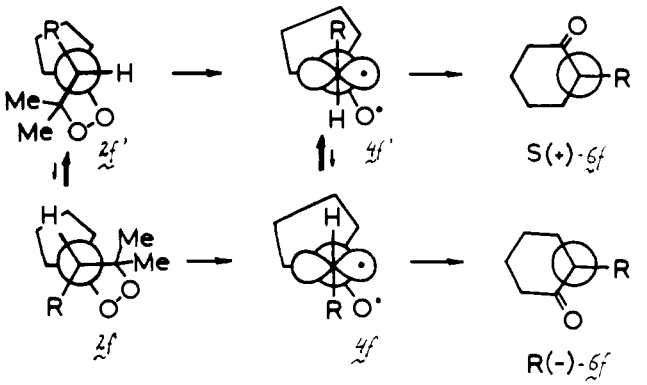
Mechanistic Interpretations. Analogous to our previous mechanistic work on the thermolysis and photolysis of β-peroxylactones,[9] we envisage the three activated complexes **17A–C**



for the formation of the rearrangement ketones **6** in the decomposition of the 1,2-dioxolanes **2**. The structure-reactivity interplay, exhibited in the kinetics of the thermolysis of the tetramethyl system **2a** and the tetraphenyl system **2e**, definitely rule out the simple oxygen-oxygen bond rupture via the activated complex **17C**, which leads to the 1,5-diradical **3**. The $\Delta H^{\ddagger}$ values would be expected to remain constant within the experimental error if this mechanism were operative, since the methyl and phenyl substituents are not directly involved in the peroxide bond cleavage.

On the other hand, the stereochemical data rule out the completely concerted three-bond fragmentation via the activated complex **17A**. This path predicts 100% inversion of

Scheme II



configuration at the chiral center (C_4 position) of the 1,2-dioxolane **2f**, affording (*R*)-(−)-2-methylcyclohexane (**6f**).[30] Instead, 91.6% racemized (*S*)-(+)-2-methylcyclohexanone (**6f**) is formed. Thus, the chiral center at the C_4 position must become free prior to rearrangement in order to account for the extensive racemization. The two-bond fragmentation of the 1,2-dioxolane via the activated complex **17B** leads to the 1,3-diradical **4**, which accommodates best our present experimental data. For example, rotational isomerization of the 1,3-diradical **4** is expected to lead to extensive racemization as illustrated by Newman projections in Scheme II. Since in rotamer **4f** methyl-oxyl interaction is minimized, the (*S*)-(+)-**6f** isomer should predominate over the (*R*)-(−)-**6f** isomer, as is observed.

This mechanism also accounts nicely for the kinetic data. Formation of the 1,3-diradical **4** is expected to be quite endothermic and the activated complex **17B** should be productlike. Consequently, the degree of deketonation in the transition state should be more extensive for the stabler ketone leaving group. The experimental leaving group ability $Ph_2C{=}O$ > PhMeC=O > $Me_2C{=}O$ also substantiates the proposed mechanism. Furthermore, the $\Delta H^{\ddagger}$ should be lower for loss of $Ph_2C{=}O$ compared to loss of $Me_2C{=}O$. The respective values of 22 and 27 kcal bear this out. The lower $\Delta H^{\ddagger}$ for the tetraphenyl system **2e** is offset by the more negative $\Delta S^{\ddagger}$ since molecular mobility is more restricted in the activated complex.[28] The experimental values, −24 and −31 gibbs/mol, confirm this trend.

The unusually high and negative $\Delta S^{\ddagger}$ needs some speculation. In view of the flexibility of the five-membered ring due to facile pseudorotation, only very specific conformations are appropriate in lining the molecule up for deketonation. Of the many possible conformations, the probability is low that a particular conformation which is active in unzipping the 1,2-dioxolane via the activated complex is achieved. The very negative $\Delta S^{\ddagger}$ values might be explained in terms of this low probability factor.

The lack of a solvent effect on the thermolysis kinetics (cf. Table IV) reveals that the 1-oxatrimethylene species **4** has

indeed predominant 1,3-diradical rather than 1,3-dipolar character, i.e., structure **4**-DR prevails over structure **4**-DP. If the dipolar structure **4**-DP were important, the rate of thermal deketonation should have been substantially greater in acetonitrile vs. benzene.

Of considerable mechanistic relevance is the preferred methyl over phenyl migration in the thermolysis as well as photolysis. Certainly in carbonium ion[31] and also in free radical[32] rearrangements aryl outweighs alkyl migration. The only other cases reporting such unusual migratory aptitudes concern the thermolysis of β-peroxylactones[29] and the photolysis of α,β-epoxy ketones.[33] In both cases the migratory preference of methyl over phenyl was explained in terms of oxyl site fragmentation in the respective diradicals as driving force. Analogously we rationalize this unusual migratory aptitude in the 1,3-diradical **4**.

Interesting is the observation that the preferential migratory aptitude of methyl vs. phenyl increases with increasing leaving group ability. Since factors which enhance diradical over dipolar character in the 1-oxatrimethylene are expected to facilitate methyl migration, the greater the ease of deketonation, the greater the 1,3-diradical character in the 1-oxatrimethylene species. Thus, since rearrangement of the 1-oxatrimethylene may be viewed as a case of intramolecular fragmentation, it should not be surprising that the ease of rearrangement vs. cyclization increases with increasing leaving group ability or degree of phenyl substitution. In other words, the greater the diradical character in the 1-oxatrimethylene, the more difficult is cyclization since fragmentation is enhanced.

In conclusion our experimental data for the thermolysis of 1,2-dioxolanes are best explained in terms of two-bond cleavage leading to the 1-oxatrimethylene diradical. The resulting 1,3-diradical is converted into stable products by rearrangement, cyclization, or fragmentation. A similar photolysis mechanism applies, but quantum yield data will be essential to substantiate more rigorously the 1,3-diradical pathway.

Our present results should be of considerable help in understanding the thermal and photochemical behavior of prostaglandin endoperoxides. A subsequent paper deals with the thermolysis and photolysis of 1,2-dioxanes as prostanoid endoperoxide model compounds.[34]

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