hexane. A ^1H NMR spectrum of the resulting pale yellow oil (1.75 g) indicated the presence of 2-Cl and 1-Cl in a ratio of 4:1.

Treatment of 6-Chloro-2,3:8,9-dibenzobicyclo[3.2.2]nona-2,6,8-trien-*exo*-4-ol (1-OH) with Triphenylphosphine–Carbon Tetrachloride. 1-OH[7] (1.08 g, 4.00 mmol) was dissolved in 7 mL of carbon tetrachloride and 1.06 g (4.0 mmol) of triphenylphosphine was added. The solution was heated at 65–70 °C for 36 h. The reaction mixture was cooled and filtered. The yellow solution was chromatographed over a silica gel column and eluted with hexane. The solution was evaporated to dryness and crystallized from 95% ethanol, producing 0.80 g (70%) of a white crystalline solid (2-Cl): mp 113 °C; ^1H NMR ($CDCl_3$) δ 7.13–7.67 (m, 8, aromatic), 6.96 (dd, 1, H-7, $J_{7,1}$ = 7.3 Hz, $J_{7,5}$ = 2 Hz), 5.60 (d, 1, H-4, $J_{4,5}$ = 4 Hz), 4.38 (d, 1, H-1, $J_{1,7}$ = 7.3 Hz), 4.13 (dd, 1, H-5, $J_{5,4}$ = 4 Hz, $J_{5,7}$ = 2 Hz). Anal. Calcd for $C_{17}H_{12}Cl_2$: C, 71.12; H, 4.18. Found: C, 71.06; H, 4.18.

In a similar experiment, the crude reaction mixture was analyzed (^1H NMR) and found to contain 80% 2-Cl and 20% 1-Cl.

Treatment of 6-Chloro-4-deuterio-2,3:8,9-dibenzobicyclo[3.2.2]nona-2,6,8-trien-*endo*-4-ol with Triphenylphosphine–Carbon Tetrachloride–Acetonitrile. The alcohol[7] (20-OH) (500 mg, 1.9 mmol) was dissolved in 8 mL of carbon tetrachloride–acetonitrile (1:1 v/v) and triphenylphosphine (655 mg, 2.50 mmol) was added. The solution was stirred for 2 h at room temperature. A preparative scale TLC was run (silica gel–10% tetrahydrofuran–hexane) on the product to remove triphenylphosphine oxide. Evaporation of solvent gave 410 mg (82%) of a yellow oil which by ^1H NMR integration of resonances at δ 4.13 and δ 4.27 contained 25% 20-Cl and 75% 21-Cl. The oil was crystallized from carbon tetrachloride to produce 250 mg (50%) of a white solid (21): mp 130–132 °C; ^1H NMR ($CDCl_3$) δ 7.10–7.65 (m, 8, aromatic), 6.96 (dd, 1, H-7, $J_{7,1}$ = 7.2 Hz, $J_{7,5}$ = 2 Hz), 4.40 (d, 1, H-1, $J_{1,7}$ = 7.2 Hz), 4.27 (d, 1, H-5, $J_{5,1}$ = 2 Hz).

Mixture melting point and spectral comparison with the nondeuterated chloride (1-Cl) proved this compound to be 21-Cl.

Acknowledgments. This work was supported in part by Grant CA-13199, awarded by the National Cancer Institute, Department of Health, Education and Welfare, and in part by National Science Foundation Grant CHE74-24348.

Registry No.—1-OH, 20887-64-3; 1-Cl, 64600-09-5; 2-Cl, 64626-00-2; 3-OH, 20851-76-7; 5-OH, 64600-10-8; 5-OAc, 64600-11-9; 6-OH, 54647-01-7; 6-Cl, 54647-00-6; 6-OAc, 64600-12-0; 7-OH, 64626-01-3; 10, 64600-13-1; 11, 64600-14-2; 20-OH, 64600-15-3; 21-Cl, 64600-16-4; thionyl chloride, 7719-09-7; 3-chloro-6,7-benzobicyclo[3.2.1]octa-3,6-dien-2-one, 57020-95-8; silver acetate, 563-63-3; carbon tetrachloride, 56-23-5; triphenylphosphine, 603-35-0.

References and Notes

(1) Paper 85: S. J. Cristol, G. O. Mayo, and J. P. Kochansky, *J. Org. Chem.*, **42**, 1131 (1977).
(2) L. Horner, H. Oediger, and H. Hoffmann, *Ann.*, 626, 26 (1959).
(3) (a) H. Hoffmann, L. Horner, H. P. Wippel, and D. Michael, *Chem. Ber.*, **95**, 523 (1962); (b) G. A. Wiley, R. L. Hershkowitz, B. M. Rein, and B. C. Chung, *J. Am. Chem. Soc.*, **86**, 964 (1964); (c) G. A. Wiley, B. M. Rein, and R. L. Hershkowitz, *Tetrahedron Lett.*, 2509 (1964); (d) J. P. Schaefer and D. S. Weinberg, *J. Org. Chem.*, **30**, 2635 (1965); (e) J. P. Schaefer and D. S. Weinberg, *ibid.*, **30**, 2639 (1965); (f) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Wiley, New York, N.Y., 1967, Vol. I, p 1247.
(4) (a) J. M. Downie, J. B. Holmes, and J. B. Lee, *Chem. Ind.*, 900 (1966); (b) J. B. Lee, *J. Am. Chem. Soc.*, **88**, 3440 (1966); (c) for a review, see: R. Appel, *Angew. Chem., Int. Ed. Engl.*, **14**, 801 (1975).
(5) (a) R. G. Weiss and E. I. Snyder, *Chem. Commun.*, 1358 (1968); (b) R. G. Weiss and E. I. Snyder, *J. Org. Chem.*, **35**, 1627 (1970); (c) R. G. Weiss and E. I. Snyder, *ibid.*, **36**, 403 (1971); (d) E. I. Snyder, *ibid.*, **37**, 1466 (1972); (e) R. Aneja, A. P. Davies, and J. A. Knaggs, *Tetrahedron Lett.*, 67 (1974).
(6) See, among others: S. J. Cristol, G. O. Mayo, and G. A. Lee, *J. Am. Chem. Soc.*, **91**, 214 (1969); S. J. Cristol, G. A. Lee, and A. L. Noreen, *ibid.*, **95**, 7067 (1973).
(7) S. J. Cristol, R. M. Sequeira, and G. O. Mayo, *J. Am. Chem. Soc.*, **90**, 5564 (1968).
(8) (a) H. Tanida, K. Tori and K. Kitahonoki, *J. Am. Chem. Soc.*, **89**, 3212 (1967); (b) S. J. Cristol and R. M. Strom, unpublished work.
(9) Such compounds have been noted earlier.[3b,5c,e]
(10) It is of considerable interest that Aneja and co-workers[5e] report that treatment of cholesterol with the reagent at 20 °C leads to large amounts of a phosphorane which they believe is that of 3,5-cyclo-6β-cholestanol. It is known,[11] of course, that derivatives of the latter alcohol are greatly unstable thermodynamically with respect to those of cholesterol. If this result is correct, and if the phosphorus derivative is similar to other derivatives of the alcohol, some mechanism for the formation of the alkoxycholorotriphenylphosphorane other than one involving simple replacement of chlorine on phosphorus by oxygen must be involved. Put another way, it must be necessary to assume that carbon–oxygen cleavage in the alcohol *precedes* the formation of the alkoxyphosphorane. We are at a loss to suggest how this could be true.
(11) S. Winstein and E. M. Kosower, *J. Am. Chem. Soc.*, **81**, 4399 (1959), and references therein.
(12) (a) F. F. Caserio, G. E. Dennis, R. H. De Wolfe, and W. G. Young, *J. Am. Chem. Soc.*, **77**, 4182 (1955); (b) S. H. Sharman, F. F. Caserio, R. F. Nystrom, J. C. Leak, and W. G. Young, *ibid.*, **80**, 5965 (1958); (c) P. B. D. de la Mare in P. de Mayo, "Molecular Rearrangements", Interscience, New York, N.Y., 1963, p 82.
(13) (a) R. E. Kepner, S. Winstein, and W. G. Young, *J. Am. Chem. Soc.*, **71**, 115 (1949); (b) W. G. Young, I. D. Webb, and H. L. Goering, *J. Am. Chem. Soc.*, **73**, 1076 (1951); (c) see ref 10c, p 33.
(14) Whether the pentavalent phosphorus compounds are best considered as pentacoordinated phosphoranes or as phosphonium chlorides seems still to be in question although recent papers favor the latter.[4c,15]
(15) J. B. Lambert and H-n. Sun, *J. Org. Chem.*, **42**, 1315 (1977).
(16) Z. Goldschmidt and U. Gutman, *Tetrahedron*, **30**, 3327 (1974).
(17) Reference 3f, p 142.

Prostanoid Endoperoxide Model Compounds: Preparation of 1,2-Dioxolanes from Cyclopropanes[1]

Waldemar Adam,*[2] Arnoldo Birke, Carlos Cádiz,[3a] Simón Díaz, and Augusto Rodríguez[3b]

Department of Chemistry, University of Puerto Rico, Río Piedras, Puerto Rico 00931

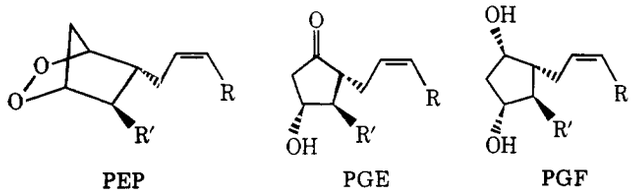
Received August 22, 1977

A synthesis of 1,2-dioxolanes from cyclopropanes, which potentially could be adapted to prepare prostanoid endoperoxide model compounds, is reported. Cyclopropanes with 1-aryl, 1,1-diaryl, and 1-alkyl-1-aryl substituents, readily prepared by 1,1-dichlorocyclopropanation of the corresponding olefins with chloroform and sodium hydroxide under tetraalkylammonium chloride phase-transfer catalysis and subsequent sodium metal/*tert*-butyl alcohol in THF reduction, were hydroperoxybrominated with *N*-bromosuccinimide or 1,3-dibromo-5,5-dimethylhydantoin. The labile γ-hydroperoxy bromides were subsequently cyclized into their respective 1,2-dioxolanes with silver oxide. The substitution pattern of the original olefin in this sequence dictates the substitution pattern of the resulting 1,2-dioxolane.

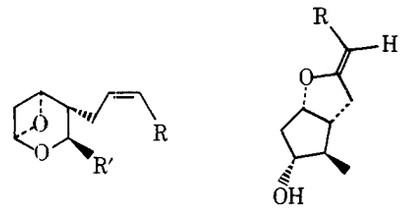
Prostaglandin endoperoxides (PEP) serve as biosynthetic precursors to the physiologically potent prostaglandins PGF and PGE,[4] thromboxane A_2,[5] and prostacyclin.[6] So far these biologically important intermediates have been accessible through natural sources, but isolation and purification have been tedious and limiting in view of the labile nature of the endoperoxides and their scarce abundance.[7] In fact, until recently even the basic endoperoxide skeleton, i.e., the 2,3-dioxobicyclo[2.2.1]heptane ring system, was unknown. We prepared[8] this novel bicyclic peroxide by in situ, selective

0022-3263/78/1943-1154$01.00/0

diimide reduction of cyclopentadiene endoperoxide (eq 1, path a), Salomon and Salomon[9] by peroxide bond transfer from bis(trialkylstannyl) peroxide to the ditriflate of 1,3-dihydroxycyclopentane (eq 1, path b), and Porter and Gilmore[10]



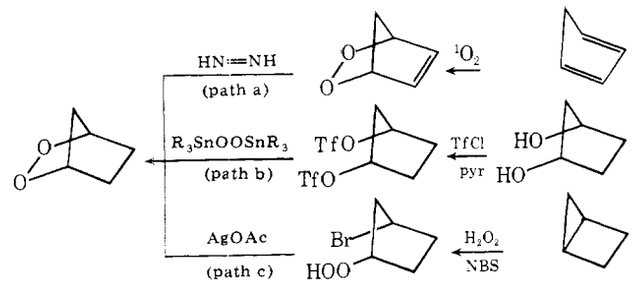
PEP PGE PGF



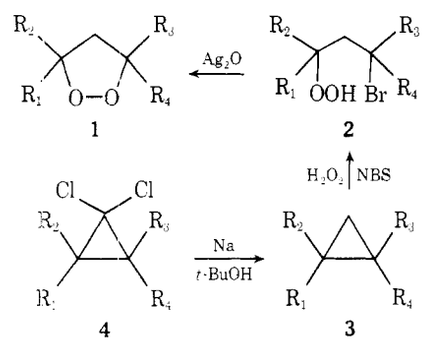
thromboxane A_2 prostacyclin

by bicyclization of 3-bromocyclopentyl hydroperoxide with silver acetate (eq 1, path c).

We also reported on the latter synthetic route (eq 1, path c, with silver oxide instead of silver acetate) earlier;[11] however, we found the hydroperoxybromination reaction of bicyclo[2.1.0]pentane and the subsequent bicyclization with silver oxide erratic, affording the impure and labile endoperoxide product in low yield. In view of our interest in prostanoid



endoperoxide model compounds,[12] we decided, therefore, to investigate in detail the hydroperoxybromination of cyclopropanes **3** and the cyclization of the γ-hydroperoxy bromides



2, to assess whether cyclopropanes **3** could serve as efficient and convenient synthons for the preparation of the simpler 1,2-dioxolanes **1**. The synthetic strategy is outlined in eq 2. Herewith we report our results on this sequence.

Experimental Section

Melting points, taken on a Thomas-Hoover melting point apparatus, and boiling points are not corrected. Refractive indices were measured on a Bausch and Lomb refractometer, supplied with a Haake temperature regulator. Infrared spectra were taken on a Perkin-Elmer Model 237 Infracord and ^1H-NMR spectra on a Hitachi Perkin-Elmer R-24B spectrometer. Elemental analysis were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Reagents and solvents were purchased from standard commercial sources and when necessary purified to match literature physical data. The olefin starting materials were either purchased or prepared according to literature procedures and purified to match reported physical and spectral data.

1,2-Dioxolanes 1 were prepared and purified according to the general method outlined below:

In a 100 mL, one-necked, round-bottomed flask, provided with magnetic spinbar, was placed ca. 20 mmol of freshly prepared and purified γ-hydroperoxy bromide **2** contained in 50 mL CCl_4 (A.R.) and cooled to 0 °C by means of an ice bath. The reaction flask was protected from light by wrapping with aluminum foil and while the solution was being magnetically stirred and cooled with an ice bath, ca. 40 mmol of freshly precipitated and thoroughly water-washed silver oxide was added all at once and the reaction progress of the heterogeneous mixture was monitored by following the hydroperoxy band in the 3500–3200-cm^{-1} region of the infrared. After completion of the reaction (usually 1–7 h), the silver bromide was removed by filtration and the solvent was rotoevaporated at 0–5 °C (10 mm) and the crude product purified by column chromatography on Silica Gel (ca. 1:100 ratio of substrate to adsorbant) at −20 °C, eluting with hexane and/or bulb-to-bulb distillation at the minimum possible bath temperature. When feasible as for 1,2-dioxolanes **1a** and **1c**, rigorous purification was achieved through fractional recrystallization from hexane and sublimation. The results are summarized in Table I.

γ-Hydroperoxy bromides 2 were prepared and purified according to the general method outlined below:

A stoppered 50-mL Erlenmeyer flask, provided with magnetic spinbar, was charged with 10 mmol of cyclopropane **3** in 20 mL of anhydrous ether and cooled to 0 °C by means of an ice bath. The flask was protected from light by wrapping with aluminum foil and while the solution was being stirred 4 mL of 98% H_2O_2 (CAUTION!) was added by means of a CHENG-tube.[13] To this cooled and stirred mixture was added by means of a spatula in portions of 10 mmol of brominating agent, either *N*-bromosuccinimide (NBS) or 1,3-dibromo-5,5-dimethylhydantoin (DDH), waiting for disappearance of the yellow bromide color between additions. After complete addition (2–5 days), intermittantly storing the reaction flask in the refrigerator (0–5 °C) overnight to avoid detrimental warm-up, the reaction mixture was washed with cold water (3 × 25 mL), with cold saturated $NaHCO_3$ (1 × 15 mL), with cold saturated $(NH_4)_2SO_4$ (1 × 15 mL), and finally again with cold water (2 × 20 mL), always placing crushed ice into the separatory funnel to prevent warm-up. The ether layer was dried over anhydrous $MgSO_4$ (60 min at 0–5 °C), the solvent was rotoevaporated (0–5 °C (10–15 mm)), and the crude product was immediately chromatographed on methanol-deactivated silica gel (ca. 1:100 ratio of substrate to adsorbant) at −10 °C, eluting with hexane–ether (19:1) and collecting fractions on the onset of a positive KI test by monitoring the eluant periodically. Relatively pure fractions (better than 80% by iodometry) were combined and rechromatographed affording material of better than 90% (by iodometry). Attempts to purify the material further by fractional low-temperature recrystallization, or column chromatography on silica gel or alumina, or DABCO precipitation led to decomposition. On storing neat in the freezer the hydroperoxides deteriorated by turning brown within a few days, but stored as CCl_4 solutions they could be preserved for longer periods. The results are summarized in Table II.

Cyclopropanes 3a, 3b, and 3d were prepared according to the general procedure (method A) outlined below:

A 1000-mL, three-necked, round-bottomed flask, provided with a reflux condenser, and efficient mechanical stirrer, was charged with 80 mmol of metallic sodium, ca. 500 mmol of *tert*-butyl alcohol, and 200 mL of THF. While stirring, 60 mmol of dichlorocyclopropane **4** was added in portions and the mixture was vigorously refluxed and high-speed stirred for ca. 60 h. To destroy the large excess of sodium metal, small portions (2 mL) of water were added while stirring and cooling the reaction vessel by means of an ice bath. The reaction mixture was extracted with hexane (3 × 100 ml), the combined extracts were washed with water (1 × 100 mL) and dried over anhydrous $MgSO_4$, the solvent was rotoevaporated (ca. 30 °C (ca. 10 mm)), and the residue was purified by fractional distillation at reduced pressure. The results are given in Table III.

Cyclopropanes 3c and 3e were isolated as by-products in the hydroperoxybromination of cyclopropanes **3b,d** by column chromatography on silica gel at 0 °C of the crude reaction mixture, collecting hexane-eluted fractions until appearance of a positive KI test for peroxide. The combined hexane eluants were rotoevaporated (ca. 30 °C (20 mm)) and the product was purified by recrystallization (**3c**) or fractional distillation (**3e**). An analytical sample of **3c** was prepared by preparative GC, using a 6 ft × ¼ in. stainless steel column packed

Table I. Yields and Physical and Spectral Properties of 1,2-Dioxolanes 1[a]

	Registry no.	R_1	R_2	R_3	R_4	Crude yield, %	bp, °C (mm)	NMR (CCl_4, Me_4Si) Type	δ, ppm	No. of H	Multiplicity (J, H_z)	IR (CCl_4) ν_{max},[b] cm^{-1}
1a	64884-60-2	Ph	Ph	H	H	93	mp 85–86[c]	$R_1 + R_2$	6.8–7.3	10	m	3085 (m), 3065 (s), 3025 (s), 2995 (m), 2965 (m), 2877 (s), 1592 (w), 1487 (s), 1444 (s), 1025 (m), 1003 (m)
								$R_3 + R_4$	4.05	2	t (6.7)	
								CH_2	3.08	2	t (6.7)	
1b	64884-61-3	Ph	Me	H	H	94	66–68 (0.2)[c]	R_1	7.0–7.4	5	m	3080 (m), 3055 (m), 3025 (m), 2978 (vs), 2925 (s), 2875 (s), 1598 (w), 1480 (s), 1445 (vs), 1368 (s), 1280 (s, broad)
								$R_3 + R_4$	3.8–4.2	2	m	
								CH_2	2.4–2.9	2	m	
								R_2	1.54	3	s	
1c	64884-62-4	pBrPh	Me	H	H	91	mp 63.5–64[c]	R_1	7.39; 7.26	4	AB (9)	3085 (w), 3025, 2980 (s), 2935 (s), 2870 (s), 1590 (m), 1482 (vs), 1448 (s), 1278 (s, broad)
								$R_3 + R_4$	3.9–4.2	2	m	
								CH_2	2.5–2.9	2	m	
								R_2	1.54	3	s	
1d	64884-63-5	Ph	H	H	H	72	50–55 (10^{-3})[d]	R_1	7.20	5	s	3060 (s), 3030 (s), 2990 (s), 2955 (s), 2910 (s), 2875 (vs), 1600 (m), 1485 (s), 1450 (vs), 1360 (m), 1325 (m), 1310 (m), 1280 (m)
								R_2	5.04; 5.16	1	AB (6.0)	
								$R_3 + R_4$	4.15	2	t (7.0)	
								CH_2	2.2–3.2	2	m	
1e	64884-64-6	pBrPh	H	H	H	86	*d*	R_1	7.04; 7.32	4	AB(9.9)	3080 (w), 3060 (w), 3025 (m), 2990 (s), 2955 (s), 2930 (s), 2875 (vs), 1485 (s), 1400 (s), 1068 (s)
								R_2	5.07; 4.98	1	AB(6.0)	
								$R_3 + R_4$	4.04	2	t (6.6)	
								CH_2	3.1–2.3	2	m	

[a] No parent ions could be observed on mass spectral analysis. [b] Relative intensities are given as very strong (vs), strong (s), medium (m), and weak (w). [c] Satisfactory elemental analyses. [d] Ca. 90% pure (by NMR) after low temperature silica gel chromatography; resisted all attempts of further purification by fractional distillation, low temperature crystallization, or gas chromatography.

Table II. Yields and Spectral Properties of γ-Hydroperoxy Bromides 2

	Registry no.	R_1	R_2	R_3	R_4	Brominating agent[a]	Yield, %	Iodide[b] titer, %	NMR (CCl_4, Me_4Si) Type	δ, ppm	No. of H	Multiplicity (J, Hz)	IR (CCl_4)[c] ν_{max}, cm^{-1} OOH	C–O
2a	64884-65-7	Ph	Ph	H	H	NBS	60	95	$R_1 + R_2$ + OOH	7.02–7.48	11	m	3500–3700 (m)	1070 (m)
									$R_3 + R_4$ + CH_2	2.7–3.5	4	m		
2b	64884-66-8	Ph	Me	H	H	DDH	50	91	R_1	7.07	5	s (broad)	3590–3200 (m)	1080 (s)
									OOH	3.95	1	s (broad)		
									$R_3 + R_4$	3.18	2	t (6.6)		
									CH_2	2.37	2	t (6.6)		
									R_2	1.50	3	s		
2c	64884-67-9	pBrPh	Me	H	H	DDH	65	92	R_1	7.00; 7.25	4	AB (9.0)	3570–3200 (m)	1078 (s)
									$R_3 + R_4$	3.16	2	t (10)		
									CH_2	2.31	2	t (10)		
									R_2	1.50	3	s		
2d	64884-68-0	Ph	H	H	H	NBS	50	96	OOH	7.53	1	s (broad)	3550–3300 (m)	1020 (m)
									R_1	7.00	5	s (broad)		
									R_2	5.02; 4.80	1	AB (5.7)		
									$R_3 + R_4$	3.0–3.2	2	m		
									CH_2	1.7–2.4	2	m		
2e	64884-69-1	pBrPh	H	H	H	NBS	85	92	OOH	8.13	1	s (broad)	3530–3130 (s)	1065 (s)
									R_1	7.33; 7.02	4	AB (10.8)		
									R_2	4.95; 4.85	1	AB (6.0)		
									$R_3 + R_4$	3.0–3.6	2	m		
									CH_2	1.8–2.6	2	m		

[a] *N*-Bromosuccinimide (NBS); 1,3-dibromo-5,5-dimethylhydantoin (DDH). [b] After silica gel chromatography at −10 °C; resisted all attempts of further purification by column chromatography or low-temperature recrystallization. [c] Relative intensities are given as strong (s), medium (m), and weak (w).

with 10% Carbowax 20M on Chromosorb W. The results are included in Table III.

1,1-Dichlorocyclopropanes 4 were prepared according to the general procedure outlined below:

A 250-mL, three-necked, round-bottomed flask, equipped with a reflux condenser and efficient mechanical stirrer, was charged with 75 mmol of olefin, 78 mmol of chloroform (A.R.), and 2.0 mmol of methyltri-*n*-caprylammonium chloride in 4.1 g of chloroform. While

Table III. Yields and Physical and Spectral Properties of Cyclopropanes 3

	Registry no.	R_1	R_2	R_3	R_4	Method[b]	Yield, %	Obsd bp, °C (mm), n_D [°C]	Reported bp, °C (mm), n_D [°C]	NMR (CCl_4, Me_4Si) Type	δ, ppm	No. of H	Multiplicity (J in Hz)
3a	3282-18-6	Ph	Ph	H	H	A	80	108–109 (1.3), 1.5850 [25]	110–111 (1.3), 1.5847 [25][c]	$R_1 + R_2$	7.08	10	s (broad)
										$R_3 + R_4 + CH_2$	1.24	4	s (broad)
3b	2214-14-4	Ph	Me	H	H	A	84	60 (13), 1.5156 [20]	66 (11), 1.5159 [20][d]	R_1	7.18	5	s (broad)
										R_2	1.39	3	s
										$R_3 + R_4 + CH_2$	0.80; 0.69	4	AB (1.8)
3c	40780-08-3	pBrPh	Me	H	H	B	87	93–94 (13.5), 1.5596 [20]	104–105 (18),[e] 1.5610 [20][f]	R_1	7.25; 6.97	4	AB (7.8)
										R_2	1.38	3	s
										$R_3 + R_4 + CH_2$	0.78; 0.70	4	AB (1.2)
3d	873-49-4	Ph	H	H	H	A	40	71.5 (22), 1.5306 [25]	69 (22), 1.5309 [25][c]	R_1	6.6–7.0	5	m
										R_2	1.5–2.0	1	m
										$R_3 + R_4 + CH_2$	0.5–1.3	4	m
3e	1124-14-7	pBrPh	H	H	H	B	68	92–93 (5.1), 1.5766 [20]	101–102 (11), 1.5773 [20][g]	R_1	7.24; 6.83	4	AB (8.4)
										R_2	1.6–2.1	1	m
										$R_3 + R_4 + CH_2$	0.5–1.1	4	m

[a] Cyclopropane skeletal deformation at ν_{max} 1020 cm^{-1} (strong). [b] Sodium reduction of 1,1-dichlorocyclopropane (method A); side product of hydroperoxybromination. [c] Reference 14a. [d] Reference 14b. [e] Reference 14c. [f] Reference 14d. [g] Reference 14e.

Table IV. Yields and Physical and Spectral Properties of 1,1-Dichlorocyclopropanes 4

	Registry no.	R_1	R_2	R_3	R_4	Yield (%)	Obsd bp, °C (mm), n_D [°C]	Reported bp, °C (mm), n_D [°C]	NMR (CCl_4, Me_4Si)[d] Type	δ, ppm	No. of H	Multiplicity (J, Hz)
4a	3141-42-2	Ph	Ph	H	H	80	mp 111–112 °C	*a*	$R_1 + R_2$	6.9–7.3	10	m
									$R_3 + R_4$	2.11	2	s
4b	3591-42-2	Ph	Me	H	H	79	92–93 (7), 1.5404 [25]	68–69 (1.3), 1.5400 [25][b]	R_1	7.06	5	s (broad)
									R_2	1.60	3	s
									R_3	1.76	1	d (6.6)
									R_4	1.47	1	d (6.6)
4d	2415-80-7	Ph	H	H	H	51	100 (10), 1.5514 [20]	103 (10), 1.5514 [20][c]	R_1	7.01	5	s (broad)
									R_2	2.75	1	t (18.6)
									$R_3 + R_4$	1.85; 1.68	2	AB (3.0)

[a] Satisfactory elemental analysis; MS (70 eV) *m/e* (rel intensity) 263 (30), 265 (18), 230 (22), 228 (14), 193 (100). [b] Reference 14f. [c] Reference 14c. [d] Cyclopropane skeletal deformation at ν_{max} 1040–1080 cm^{-1} (strong).

stirring vigorously, 40 mL of a solution of 50% aqueous NaOH was added and the two-phase mixture was stirred for 4–6 h at 50–55 °C; the exothermic reaction mixture was cooled with a water bath. The reaction mixture was extracted with ether (3 × 50 mL), the combined ether extracts were washed with water (3 × 50 mL) and dried over anhydrous $MgSO_4$, and the solvent was rotoevaporated (ca. 30 °C (ca. 10 mm)). The crude product was purified by recrystallization or fractional distillation at reduced pressure. An analytical sample of **4a** was prepared by repetitive, alternating recrystallization from hexane and sublimation (78 °C (0.15 mm)). The results are summarized in Table IV.

Discussion

The cyclopropanes **3a,b,d** required in this work were conveniently prepared in good yields by dichlorocyclopropanation (Table IV) of the corresponding olefins with chloroform and NaOH, using methyltri-*n*-caprylammonium chloride as phase transfer catalyst,[15] followed by sodium metal/*tert*-butyl alcohol dechlorination[16] in THF (Table III), as illustrated in eq 2. The *p*-bromophenylcyclopropanes **3c,e** (Table III) were isolated as by-products in the hydroperoxybromination of the corresponding cyclopropanes **3b,d.**

The last fact already brings out the problematic nature of the hydroperoxybromination of cyclopropanes **3.** While olefins hydroperoxybrominate swiftly even at −20 °C,[17] ring opening of cyclopropanes is slow at 0–10 °C even for activated cyclopropanes, requiring long reaction times (20–150 h). Higher temperatures cannot be tolerated since the labile γ-hydroperoxy bromides **2** decompose. Thus, at least one aryl substituent was essential for reasonable reactivity since monoalkylated and 1,2-dialkylated cyclopropanes were inert, while 1,1-dialkylcyclopropanes reacted too sluggishly to be useful.

Best results were obtained with 1,1-diphenylcyclopropane (**3a**), cf. Table II. The hydroperoxybromination of this substrate proceeded moderately fast (ca. 20 h) at 0 °C, thus suppressing the competing electrophilic aromatic bromination.[18] The latter process is favored at elevated temperatures; however, we found it to be quite unpredictable. Even rigorously purified reagents, substrates, and solvent and conducting the brominations in the dark gave variable amounts of aromatic bromination vs. ring opening from run to run. Careful moni-

toring of the reaction revealed that in the early stages only hydroperoxy bromides **2** were formed, provided the temperature was rigorously controlled at 0–5 °C and the brominating agent never allowed to accumulate by too fast addition. Only the stoichiometrically required amount of the brominating agent could be tolerated. Furthermore, 1,3-dibromo-5,5-dimethylhydantoin (DDH), a more powerful brominating agent, was more problematic than NBS. Molecular bromine was also used, but the liberated HBr would catalyze the decomposition of the hydroperoxybromination product **2**. Aromatic bromination did not take place when the hydrogen peroxide was left out or substituted by methanol.

The purification of the unstable γ-hydroperoxy bromides **2** presented formidable problems. They decomposed on silica gel TLC plates or on attempted precipitation as DABCO complexes.[17] Efforts to crystallize them failed, which is not surprising in view of their unsymmetrical nature. The only viable purification method, affording material of >90% purity (by iodometry), was by column chromatography on methanol-deactivated silica gel[19] at −10 °C, eluting with hexane–ether (19:1), cf. Table II. All operations, even solvent removal, had to be conducted at sub-ambient temperatures since even the chromatographically purified substances deteriorate on standing in the freezer, losing their peroxide titer within a few days. Consequently, immediately after purification the γ-hydroperoxides were cyclized.

The cyclization worked well if freshly precipitated silver oxide was used and the substrate **2** was employed immediately after chromatography. However, purification again presented problems. At room temperature these materials decomposed on attempted silica gel chromatography. Working at −20 °C and on deactivated silica gel reasonably pure (ca. 90%) 1,2-dioxolanes could be obtained which were further purified by recrystallization and sublimation or by bulb-to-bulb distillation at reduced pressure (Table I). The pure materials deteriorate on standing within a few months. This should be contrasted with the 1,2-dioxolanes with tertiary α-carbons at the peroxide linkage, which are indefinitely stable.[12a] The reason for this is, of course, the propensity of 1,2-dioxolanes with primary or secondary α-carbons to isomerize readily, as demonstrated for the prostaglandin endoperoxides.[4]

In conclusion, the synthetic sequence developed here for 1,2-dioxolanes, modelled after Kopecky's synthesis of 1,2-dioxetanes,[20] works well for 1,1-diaryl- and 1-alkyl-1-arylcyclopropanes but is already problematic for 1-arylcyclopropanes and ineffective for 1,1-dialkyl- and 1-alkylcyclopropanes. The reactivity of the bicyclo[2.1.0]pentane toward hydroperoxybromination (eq 1) is enhanced due to the additional ring strain. A definite advantage is the fact that the substitution pattern of the starting olefin dictates the substitution pattern of the final 1,2-dioxolane.

Acknowledgments are made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, the National Science Foundation (Grant CHE 72-04956-A03), and the National Institutes of Health (Grants GM-22119-02, GM-00141-02, and RR-8102-03) for support of this work. The experimental assistance of R. Ricart is gratefully appreciated. We wish to thank Dr. W. Fenical for suggesting the hydroperoxybromination sequence to us.

Registry No.—H_2O_2, 7722-84-1; NBS, 128-08-5; DDH, 77-48-5; chloroform, 67-66-3; 1,7-diphenylethene, 530-48-3; 1-methyl-1-phenylethene, 98-83-9; 1-phenylethene, 100-42-5.

References and Notes

(1) Paper 60 in the Cyclic Peroxide Series.
(2) NIH Career Development Awardee (1975–80).
(3) (a) Undergraduate Participant in the Support for University Biomedical Education (SUBE) program, funded by NIH. (b) Graduate Research Fellow in the SUBE program.
(4) M. Hamberg, J. Svenson. T. Wakabayashi, and B. Samuelson, *Proc. Natl. Acad. Sci. U.S.A.*, **71**, 345 (1974).
(5) G. B. Kolata, *Science*, **190**, 770 (1975).
(6) R. A. Johnson, P. R. Morton, J. H. Kinner, R. R. Gorman, J. G. McGuire, F. F. Sun, N. Whittacker, S. Bunting, J. Salmon, and J. R. Vane, *Prostaglandins*, **12**, 915 (1976).
(7) (a) N. S. Crossley, *Chem. Ind. (N.Y.)*, 334 (1976); (b) B. Samuelsson, E. Granstrom, K. Green, M. Hamberg, and S. Hammarström, *Annu. Rev. Biochem.*, **44**, 669 (1975).
(8) W. Adam and H. Eggelte, *J. Org. Chem.*, **42**, 3987 (1977).
(9) R. G. Salomon and M. F. Salomon, *J. Am. Chem. Soc.*, **99**, 3501 (1977).
(10) N. A. Porter and D. W. Gilmore, *J. Am. Chem. Soc.*, **99**, 3503 (1977).
(11) W. Adam, A. Birke, and R. Paoli, "8th Junior Technical Meeting", August 30, 1975, sponsored by the Puerto Rico Section of the American Chemical Society.
(12) (a) W. Adam and N. Durán, *J. Am. Chem. Soc.*, **99**, 2729 (1977); (b) W. Adam and J. Sanabia, *ibid.*, **99**, 2735 (1977); (c) W. Adam and H. J. Eggelte, *Angew. Chem.*, **89**, 762 (1977).
(13) W. Adam, J.-C. Liu, and O. Rodriguez, *Org. Photochem. Synth.*, **2**, 13 (1976).
(14) (a) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959); (b) C. Gilbert and J. Seyden-Penne, *Bull. Soc. Chim. Fr.*, 2410 (1970); (c) Yu. S. Shabarov, S. S. Mochalov, and G. V. Alekakhu, *Zh. Org. Khim.*, **9**, 1187 (1973); (d) M. Horak, S. Smejkal and S. Farker, *Collect. Czech., Chem. Commun.*, **28**, 2280 (1963); (e) Yu. S. Shabarov, R. Ya. Levina, V. K. Potopov, A. M. Osipov, and E. G. Treshchora, *Zh. Org. Khim.*, **30**, 3874 (1960); *Chem. Abstr.*, **55**, 25808i (1955); (f) D. Seyferth, J. M. Burlitch, R. Y. Monarz, J. Y. Pui, H. D. Simmons, A. J. H. Treiber, and S. D. Dowd, *J. Am. Chem. Soc.*, **87**, 4259 (1965); (g) W. J. Dale and P. E. Schwartzentruber, *J. Org. Chem.*, **24**, 955 (1957).
(15) M. Makoza and M. Warzyniewics, *Tetrahedron Lett.*, 4659 (1962).
(16) P. G. Gassman and J. L. Marshall, "Organic Syntheses", Collect. Vol. 5, Wiley, New York, N.Y., 1973, p 427.
(17) K. R. Kopecky, J. E. Filby, C. Mumford, P. A. Lockwood, and J. Y. Ding, *Can. J. Chem.*, **53**, 1103 (1975).
(18) (a) E.-G. Kleinschmidt and H. Brauninger, *Pharmazie*, **24**, 87, 94 (1969); (b) F. Dewhurst and P. K. J. Shah, *J. Chem. Soc. C*, 1737 (1970).
(19) E. R. Katzenellenbogen, K. Dobriner, and T. H. Kritchevsky, *J. Biol. Chem.*, **207**, 315 (1954).
(20) K. R. Kopecky, J. E. Filby, C. Mumford, P. A. Lockwood, and J.-Y. Ding, *Can. J. Chem.*, **53**, 1103 (1975).