standard, dissolved in 25 mL of dichloromethane. Reactions to establish reactivity at pH >10, in light vs dark reactions, and in runs conducted without catalyst employed organic phases consisting $1-3 \times 10^{-3}$ mol of substrate with equal molar amounts of 1,4-dichlorobenzene as internal standard, in 50 mL of CH_2Cl_2.

Comparative Reactions of Substituted Bromobenzenes (Table I). Substrates (1×10^{-3} mol) and equal molar amounts of bromobenzene and internal standards were dissolved in 50 mL of dichloromethane and stirred magnetically with 200 mL (0.1 mol) of hypochlorite containing 0.2 g (6×10^{-4} mol) of PTC in three-necked 250-mL round-bottom flasks. The pH's of aqueous layers were monitored and adjusted continuously to maintain pH 8-9 for periods indicated. The identity of 1-chloro-2-(4-chlorophenyl)-2-methylpropane as a byproduct from reaction of 4-bromo-*tert*-butylbenzene (**1f**) was indicated by gas chromatography/mass spectrometry.

The above procedure, modified by replenishment of the aqueous hypochlorite layer and catalyst twice during stirring for 2 weeks at pH 7.5-9, resulted in conversion of over 90% of 1,4-dibromobenzene to a 6:1 mixture of 1,4-dichlorobenzene and 1-bromo-4-chlorobenzene. Analysis of reactions in progress showed initial buildup of the bromochloro intermediate followed by its diminishment as the dichloro product accumulated.

Acknowledgment. The support of this work by a Chemistry Department Research Grant from the Robert A. Welch Foundation sincerely is appreciated. Further acknowledgement is made to the Donors of The Petroleum Research Fund, administered by the American Chemical Society, for the partial support of this research. We thank Dr. Bill Hendrickson of the University of Dallas and Dr. Andy Armstrong of Armstrong Forensic Laboratory for GC/MS characterization of products from 4-bromo-*tert*-butylbenzene and 1,4-dibromobenzene, respectively. We also are grateful to the NSF for providing LC instrumentation under RUI Grant CHE8312738.

Registry No. **1a**, 108-86-1; **1b**, 586-78-7; **1c**, 90-90-4; **1d**, 108-37-2; **1e**, 106-39-8; **1f**, 3972-65-4; **1g**, 101-55-3; **1h**, 92-66-0; $ClCH_2C(CH_3)_2C_6H_4$-*p*-Cl, 13099-56-4; BrC_6H_4-*p*-Br, 106-37-6; ClC_6H_4-*p*-Cl, 106-46-7; ClC_6H_4-2-Br, 106-39-8; Clorox, 7681-52-9.

Synthesis of Pentasubstituted 3-Hydroxy-1,2-dioxolanes

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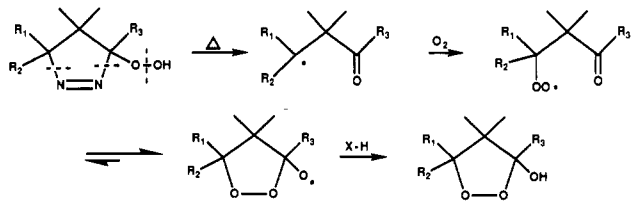
Introduction

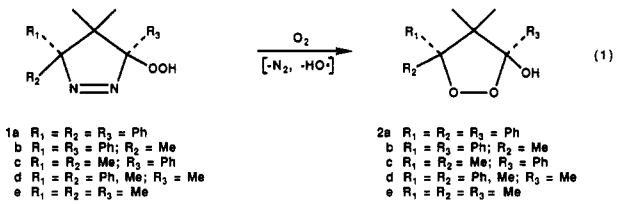
Five-membered cyclic peroxides are of synthetic and mechanistic importance.[1-3] Several examples of 3-hydroxy-1,2-dioxolanes (hemiperketals) and related ring systems have been found as natural products.[2,4] Synthetic routes to 3-hydroxy-1,2-dioxolanes and closely related ring systems usually involve the reaction of singlet oxygen[5] or hydrogen peroxide[6] with α,β-unsaturated carbonyl compounds. Autoxidation or photooxidation of cyclopropanols has been shown[7] to produce hemiperketals in several specialized examples. We report here the synthesis of a series of 3,4,4,5,5-pentasubstituted-3-hydroxy-1,2-dioxolanes via O_2 trapping of intermediates generated during the thermolysis of cyclic α-azo hydroperoxides.

Scheme I



Results and Discussion

The thermal decomposition of a series[8] of cyclic α-azo hydroperoxides **1a-e** in benzene or acetone in the presence of 100% O_2 (at one atmosphere) yielded the corresponding 3,4,4,5,5-pentasubstituted 3-hydroxy-1,2-dioxolanes in moderate yields (eq 1). The hemiperketals (isolated in 35-50% yields by chromatographic methods) were characterized by physical and spectral techniques. The 3-hydroxy-1,2-dioxolanes were of remarkable stability and appeared not to be in rapid equilibrium[9] with the ring-opened form. No reaction (ambient temperature) with dimethyl sulfide was observed, while reaction with trivalent phosphorus compounds required days to reach completion. ^{17}O NMR[10] data on **2b** and **2d** in CH_2Cl_2 at 25 °C (for **2b** δ 304 ± 2 ppm ($\nu_{1/2}$ = 2600 Hz) peroxy oxygens, unresolved and δ 78 ± 1 ppm ($\nu_{1/2} \approx$ 850 Hz) hydroxy oxygen; for **2d** δ 302 ± 2 ppm peroxy oxygens, unresolved and δ 74 ± 2 ppm hydroxy oxygen) also were in agreement with the closed structure. However, compound **2b** was noted to



(1)

1a $R_1 = R_2 = R_3 = Ph$
b $R_1 = R_3 = Ph$; $R_2 = Me$
c $R_1 = R_2 = Me$; $R_3 = Ph$
d $R_1 = R_2 = Ph$, Me; $R_3 = Me$
e $R_1 = R_2 = R_3 = Me$

2a $R_1 = R_2 = R_3 = Ph$
b $R_1 = R_3 = Ph$; $R_2 = Me$
c $R_1 = R_2 = Me$; $R_3 = Ph$
d $R_1 = R_2 = Ph$, Me; $R_3 = Me$
e $R_1 = R_2 = R_3 = Me$

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Table I. Data for 3,5,5-Trisubstituted 4,4-Dimethyl-3-hydroxy-1,2-dioxolanes 2a–e

no.	R_1	R_2	R_3	mp (°C) dec	% yield[a]	^{1}H NMR[b] (ppm)	^{13}C NMR[b] (ppm)	MS (70 eV)	anal calcd	anal found
2a	Ph	Ph	Ph	95–96.5	52	0.76 (s, 3 H), 1.61 (s, 3 H), 2.63 (br s, 1 H), 7.33 (m, 9 H), 7.53 (m, 4 H, 7.87 (m, 2 H)	20.6, 25.2, 62.2, 91.4, 110.7, 125.4, 127.0, 127.1, 127.2, 127.4, 127.9, 128.3, 128.4, 128.7, 137.6, 141.7, 142.2	no M^+ EI or CI	C: 79.74 H: 6.40 $C_{23}H_{22}O_3$	C: 79.80 H: 6.48
2b	Ph	Me	Ph	79–80	48	0.20 (s, 3 H), 1.36 (s, 3 H), 1.90 (s, 3 H), 3.06 (s, 1 H), 7.20–7.50 (m, 10 H)	19.2, 25.4, 26.9, 58.3, 91.2, 109.0, 125.2, 126.5, 126.8, 127.9, 128.1, 128.8, 138.3, 144.1	no M^+ EI or CI	C: 76.03 H: 7.09 $C_{18}H_{20}O_3$	C: 75.88 H: 7.16
2c	Me	Me	Ph	82–83	36	0.62 (s, 3 H), 1.18 (s, 3 H), 1.27 (s, 3 H), 1.51 (s, 3 H), 3.02 (s, 1 H), 7.35 (m, 3 H), 7.51 (m, 2 H)	19.5, 23.4, 24.0, 24.4, 57.5, 87.7, 109.0, 126.5, 128.1, 128.6, 134.5	223 $(M^+ + 1)$ Cl	C: 70.24 H: 8.16 $C_{13}H_{18}O_3$	C: 69.90 H: 7.96
2d[c]	Ph	Me	Me	90–92	38	0.57 (s, 3 H), 1.28 (s, 3 H), 1.36 (s, 3 H), 1.72 (s, 3 H), 2.73 (s, 1 H), 7.33 (m, 5 H)[c]	19.9, 20.1, 25.1, 26.1, 57.0, 90.5, 108.0, 125.8, 126.8, 127.9, 144.5[c]	205 $(M^+ + 1) - H_2O$ CI	C: 70.24 H: 8.16 $C_{13}H_{18}O_3$	C: 70.25 H: 8.24
2e	Me	Me	Me	oil	49	1.04 (s, 3 H), 1.08 (s, 3 H), 1.26 (s, 3 H), 1.32 (s, 3 H), 1.39 (s, 3 H), 2.67 (s, 1 H)	20.3, 21.0, 23.1, 23.5, 24.1, 55.9, 87.3, 108.0	160.1 (M^+/e)	C: 59.98 H: 10.15 $C_8H_{16}O_3$	C: 60.07 H: 10.07

[a] Isolated. [b] $CDCl_3$. [c] Spectral data for major isomer only (minor isomer (R_1 = Me, R_2 = Ph) 11% yield).

epimerize very slowly at 80 °C before undergoing thermolysis. α-Azo hydroperoxide, **1d**, was a mixture (80/20) with the major isomer determined to be the *cis*-3-methyl-5-phenyl compound. The resulting hemiperketal **2d** was isolated (49%) as a mixture (77/23) of isomers with the corresponding stereochemistry. Compound **2e** has been previously reported.[7c] The active oxygen content of the hemiperketals was determined to be 95 ± 2%. The data are summarized in Table I.

The mechanism for the generation of the hemiperketals is likely to be a free-radical process (see Scheme I). The thermolysis of α-azo hydroperoxides would be facilitated by concerted cleavage of the O–O bond and at least one C–N bond and would generate β-keto radicals efficiently. The induced decomposition of α-azo carbinols is closely analogous as concerted homolysis of the O–H bond and at least one C–N bond has been demonstrated.[11] Trapping of β-keto radical intermediates by O_2 will yield the corresponding peroxy radicals. Exo closure of the peroxy radicals will yield the hemiperketal radicals. Subsequent hydrogen atom abstraction from the solvent or other suitable donors will yield the hemiperketals.

The results for the oxidative thermolysis of **1b** and **1d** indicated a high degree of retention of configuration. The 3,5-substituents prefer to be cis. For example, thermolysis of the *cis*-diphenyl compound **1b** yielded the corresponding cis hemiperketal **2b** as the major product and only very minor amounts of the trans isomer. This result may reflect a stereochemical preference rather than an unusual aspect of the reaction of oxygen with the radical intermediate. It is likely that the reaction of O_2 will occur with both faces of the β-keto radical with equal probability. Ring closure of the peroxy radicals on the appropriate faces of the carbonyl group would yield the cis hemiperketal radical and would be the origin of the observed retention.

O_2 trapping of β-keto radicals generated by α-azo hydroperoxide thermolysis is efficient. Since generalized procedures have been reported[12] for the preparation of cyclic α-azo hydroperoxides, this new route is convenient and applicable to the synthesis of a variety of hemiperketals.

In conclusion, the oxidative thermolysis of cyclic α-azo hydroperoxides is a new convenient method for the synthesis of hemiperketals.

Experimental Section

All solvents were of reagent grade. Benzene was distilled over calcium hydride before use. The synthesis of the cyclic α-azo hydroperoxides[8] has been reported. The ^{1}H and ^{13}C NMR spectra were recorded on a JEOL GX-270 NMR spectrometer. IR spectra were recorded on a Bomem-Michelson 100-FT-IR spectrometer. Melting points were taken in a Thomas Hoover Uni-melt apparatus and are uncorrected. Combustion analyses were performed by Atlanta Microlabs, Atlanta, GA. The MS data were obtained at the Georgia Institute of Technology.

3,5,5-Trisubstituted 4,4-Dimethyl-3-hydroxy-1,2-dioxolanes 2a–e. The following procedure for the synthesis of hemiperketal **2a** is representative: a solution of 0.30 g (0.838 mmol) of α-azo hydroperoxide **1a** (CAUTION), 3,3,5-triphenyl-4,4-dimethyl-4,5-dihydro-5-hydroperoxy-3*H*-pyrazole, in 25 mL of benzene was placed in a Schlenk tube at ambient temperature (~22 °C). Pure oxygen gas was bubbled through the solution. After 5 h, the reaction was complete as monitored by ^{1}H NMR spectroscopy (change in upfield "methyl" for **1a**). Reaction times were shorter (1–3 h) for the less stable cyclic α-azo hydroperoxides. Acetone could be substituted for benzene as the reaction solvent with little or no effect on the yields. The less stable cyclic α-azo hydroperoxides **1c–e** were prepared in situ at low temperature and allowed to decompose slowly under an oxygen atmosphere at 22 °C. The solvent was removed under reduced pressure and the residue purified by chromatographic methods (chromatatron: $^1/_8$-in. plates; Silica Gel 60 PF_{254} containing gypsum (with fluorescent indicator); petroleum ether/ether 5% step gradient). For **2a**, 0.15 g (0.435 mmol, 52%) of a white crystalline solid were obtained after recrystallization from petroleum ether: IR (film) 3532 cm^{-1}; for **2b** IR (KBr) 3421 cm^{-1}; for **2c** IR (KBr) 3451 cm^{-1}; for **2d** IR (KBr) 3421 cm^{-1}; for **2e** IR (neat) 3465 cm^{-1}. Hemiperketal **2e** was found to be extremely volatile. Care must be taken or much of this material will be lost during concentration of the samples. The data for **2a–e** are summarized in Table I.

Active Oxygen Determination. The following procedure with slight modifications from the standard methods[13] was employed for the determination of the active oxygen content. A weighed sample (usually ~10 mg) of hemiperketal was placed in a solution

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prepared by mixing 5 mL methanol and 5 mL of aqueous 10% KI/7.2% HCl. The reaction mixture was allowed to sit in the dark for 30 min. Upon completion, the reaction mixture was titrated to end point with ~0.01 M $Na_2S_2O_3$. The results were corrected for a blank titration. The percentage of active oxygen for the hemiperketals was found to be 95 ± 2%.

^{17}O NMR Spectroscopy. The ^{17}O NMR spectra were recorded on a Varian VXR-400 spectrometer equipped with a 10-mm broad-band probe. All spectra were acquired at natural abundance at 25 °C in methylene chloride. The concentration of the compounds employed in these experiments was 0.2 M. The signals were referenced to external deionized water at 25 °C. The instrumental settings were spectral width 35 kHz, 2K data points, 90° pulse angle (40-μs pulse width) 150-μs acquisition delay, 29-ms acquisition time. Typically 40 000–100 000 scans were required. The spectra were recorded with sample spinning and without lock. The signal-to-noise ratio was improved by applying a 25–50 Hz exponential broadening factor to the FID prior to Fourier transformation. The data point resolution was improved to ±0.1 ppm by zero filling to 8K data points. The reproducibility of the chemical shift data is estimated to be better than ±2.0 ppm.

Acknowledgment is made to the National Science Foundation (CHE-9017230) for support of this research. NMR instrumentation was obtained, in part, by a NSF Equipment Grant (CHE8409599).

Registry No. **1a**, 133610-01-2; **1b**, 137363-38-3; **1c**, 133610-04-5; *trans*-**1d**, 133610-50-1; *cis*-**1d**, 133610-05-6; **1e**, 137363-39-4; **2a**, 137363-40-7; **2b**, 137363-41-8; **2c**, 137363-42-9; *trans*-**2d**, 137363-43-0; *cis*-**2d**, 137363-44-1; **2e**, 25243-43-0.

Medium-Sized Cyclophanes. 15. Bromination and Lewis Acid Catalyzed Isomerization of 8,16-Diethyl[2.2]metacyclophane[1]

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Introduction

Sato and his co-workers[2] have reported that bromination of 8,16-unsubstituted [2.2]metacyclophane (MCP = metacyclophane) with bromine in the presence of Fe powder afforded the corresponding tetrahydropyrene via an addition–elimination mechanism.[3-8]

Recently, we reported[9] that in similar bromination reactions of 8,16-dimethyl[2.2]MCP (**1a**), the isomerization and transannular cyclization product, 2,7-dimethyl-1,3,6,8-tetrabromo-4,5,9,10-tetrahydropyrene (**2**), was obtained due to the release of the strain in the molecule. This novel isomerization and transannular cyclization reaction might be attributed to the methyl groups at the 8,16-positions, which increase the strain in the molecule in comparison with the 8,16-unsubstituted [2.2]MCPs.

Therefore, we decided to investigate the substituent effects at 8,16-positions on the bromination of [2.2]MCPs.

The reaction of 8,16-diethyl[2.2]MCP (**1b**) with bromine and its treatment with Lewis acids in CCl_4 are reported in this paper.

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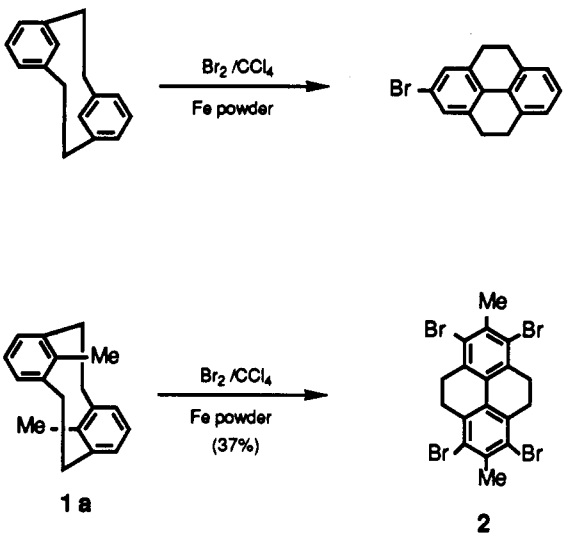
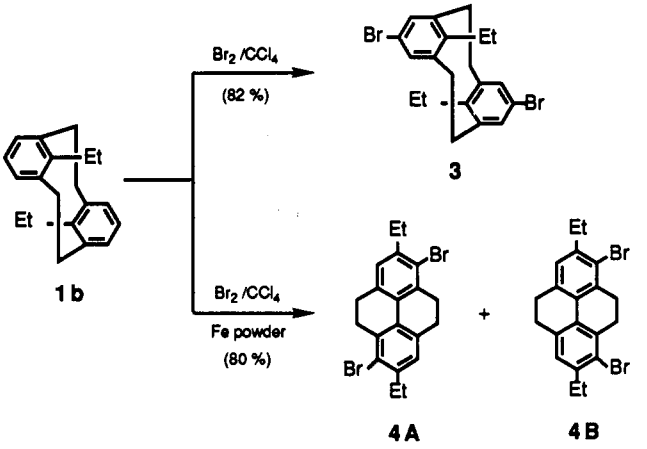
Scheme I



Scheme II



Results and Discussion

Bromination of 8,16-diethyl[2.2]MCP (**1b**) with 6 equiv of bromine at room temperature for 5 min led to 5,13-dibromo-8,16-diethyl[2.2]MCP (**3**) in 82% yield analogous to the bromination of 8,16-dimethyl[2.2]MCP (**1a**). On the other hand, bromination in the presence of Fe powder for 2 h under the same reaction conditions as described above afforded a mixture of 1,6-dibromo-2,7-diethyl- (**4A**) and 1,8-dibromo-2,7-diethyl-4,5,9,10-dihydropyrene (**4B**) in 80% yield (Scheme II). The structure of **4A** and **4B** was assigned by spectral data and elemental analysis. It seems that compound **4** might be formed by isomerization and transannular cyclization of **1b** catalyzed by $FeBr_3$, which should be produced from bromine and Fe powder present during the bromination.

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