(1 H, d, J = 2.3 Hz).
(10) A similar epoxidation occurs in the reaction of α,β-unsaturated ketones with the sodium salt of *tert*-butyl hydroperoxide: N. C. Yang and R. A. Finnegan, *J. Am. Chem. Soc.*, **80**, 5845 (1958).
(11) R. A. Johnson and E. G. Nidy, *J. Org. Chem.*, **40**, 1680 (1975).
(12) A. Mondon, *Angew. Chem.*, **64**, 224 (1952); ^{1}H NMR (60 MHz, in C_6D_6) δ 1.72 (3 H, s), 2.18 (4 H, s), 9.36 (1 H, s).
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(14) Note Added in Proof: Imidazole catalyzes the rearrangement of 1 to a mixture of **7** and **8** (1:1).

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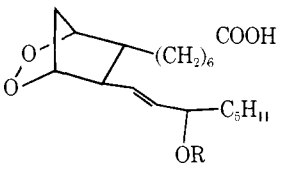
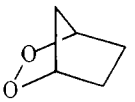
2,3-Dioxabicyclo[2.2.1]heptane

Sir:

The isolation of the two prostaglandin bicyclic endoperoxides PGG and PGH[1] has sparked considerable synthetic interest in the 2,3-dioxabicyclo[2.2.1]heptane structure. These endoperoxides have not only been identified as intermediates in prostaglandin formation, but they have also been shown to exhibit strong and independent physiological effects, as well.



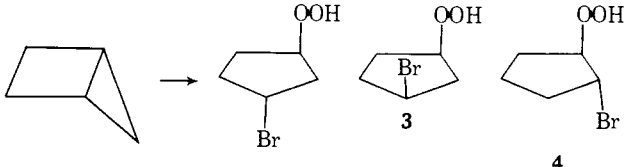
PGG, R = OH
PGH, R = H



1

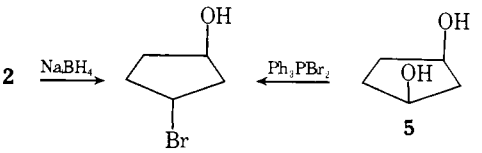
Primary or secondary dialkyl peroxides are usually prepared by the alkylation of basic hydrogen peroxide with alkylmesylates[2] or by the reaction of alkyl mesylates or halides with superoxide.[3-5] The conditions of the basic hydrogen peroxide reaction are, however, too harsh for a product endoperoxide like PGG to survive and the superoxide method has thus far failed to yield bicyclic endoperoxides. We reasoned that the conditions used for the synthesis of unstable dioxetanes[6] (β-bromohydroperoxides and silver acetate) might also be successfully employed for the synthesis of the bicyclic endoperoxide structure. We report here the successful synthesis of **1** via the reaction of silver acetate and *trans*-3-bromocyclopentane hydroperoxide.The conversion to **1** is clean and quantitative and thus provides a promising route to the prostaglandin endoperoxides.

Reaction of bicyclopentane[7] (0.027 mole) with 98% H_2O_2 (1.06 mol) and *N*-bromosuccinimide (0.03 mol) in diethyl ether at −41 °C (3 h) led to the formation of three bromohydroperoxides which could be separated by silica chromatography at −10 °C.[8] **2** and **3** were the major products formed (1:1 ratio) with **4** comprising less than 5% of the mixture. The



2 3 4

structures of **2** and **3** are supported by proton and carbon magnetic resonance spectroscopy,[9] iodometric titration, and reduction ($NaBH_4$) to the γ-bromocyclopentanols. *trans*-3-Bromocyclopentanol was prepared independently from *cis*-1,3-cyclopentanediol[10] by reaction with triphenylphosphine dibromide,[11] a reaction known to occur with inversion of configuration.[12] The γ-bromo alcohol derived from reduction of **2** was identical with that prepared from the diol in every respect.[13]

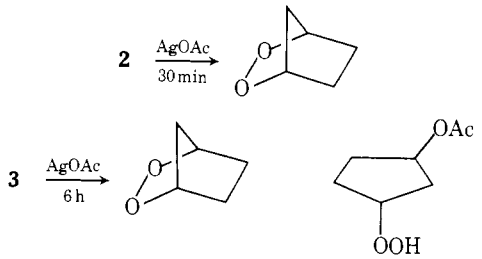


5

Reaction of **2** (3.45 mmol) in a stirred slurry (CH_2Cl_2) of silver acetate (20.5 mmol) for 30 min led quantitatively to **1** as judged by NMR. The ^{1}H NMR of this peroxide is characterized by a dominant broad singlet at δ 4.8 with the region between δ 1.6 and 2.5 being remarkably similar to that of the 2,3-diazabicyclo[2.2.1]hept-2-ene azo analogue[14] (^{1}H NMR of **1** (CCl_4) δ 1.6-2.1 (4 H, m), 2.2-2.4 (2 H, m), 4.8 (2 H, s)). The ^{13}C NMR of **1** consists of signals at 29.1, 43.8, and 78.8 ppm (reference Me_4Si), consistent with the symmetry of the molecule. **1** can be purified by bulb to bulb distillation, low temperature crystallization (pentane), or sublimation, and the white crystalline material thus purified melts at 42.0-43.5 °C dec. **1** is remarkably stable in organic solvents and a carbon tetrachloride solution of the endoperoxide has been warmed briefly to 60 °C without significant decomposition. Prolonged heating does lead to decomposition products that absorb in the carbonyl region of the infrared.

Reduction of **1** (thiourea)[15] followed by acetylation (acetic anhydride-pyridine) leads to *cis*-1,3-diacetoxycyclopentane that is identical in every respect[13] with material prepared independently from authentic *cis*-1,3-cyclopentanediol.[10]

Reaction of the *cis*-γ-bromocyclopentane hydroperoxide **3** with silver acetate occurs with a much slower rate than the reaction of **2.** Thus, after reaction of **3** with silver acetate for 4 h under conditions similar to those described for **2,** a significant amount of **3** remains. After complete consumption of **3** (6 h), **1** and a new product tentatively identified as 3-acetoxycyclopentane hydroperoxide are present in the reaction mixture.



The dramatic differences in rate and product specificity found in the reaction of **2** and **3** with silver acetate point to the involvement of the hydroperoxide group in the transition state. In particular, the hydroperoxy group appears to be assisting in the loss of bromide via an intramolecular S_N2 type transition state.

The formation of the γ-bromohydroperoxides from bicyclopentane also deserves comment. Addition of molecular bromine or chlorine to the strained bridge bond of bicyclopentane occurs with predominant formation of the trans 1,2 dihalide.[16] In the reaction reported here, hydrogen peroxide, an excellent nucleophile present in excess, presumably traps the first formed carbonium ion species before rearrangement to the stable bridged 1,2 bromonium ion can occur.

The success of the silver salt-hydroperoxide approach and the recent report[17] of organic peroxide synthesis via alkylhalides, silver salts, and hydrogen peroxide suggested that *cis*-1,3-cyclopentanedibromide,[18] **6,** might be a precursor of endoperoxide **1.** In fact, **6** can be converted to **1** in 30-40% yield by its reaction in methylene chloride with silver acetate or silver trifluoroacetate and hydrogen peroxide. Thus, 1,3 bromohy-

droperoxides or 1,3 dibromides may possibly act as precursors for authentic PGG or PGH or for other biologically active analogues.[19]

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References and Notes

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(8) The chromatographic scheme was successive elution with 400 mL each of hexane and 1, 2, 3, and 4% ether in hexane. **2** eluted primarily with the 3% ether fractions, **3** with the 4% ether fractions.
(9) **2** ^{1}H NMR (CCl_4) δ 1.8–2.3 (4 H, m), 2.3–2.5 (2 H, t), 4.2–4.9 (2 H, m), 8.65 (1 H, s); **2** ^{13}C NMR ($CDCl_3$) δ 29.09, 36.01, 43.05, 50.13, 86.10; **3** ^{1}H NMR (CCl_4) δ 1.8–2.3 (4 H, m), 2.3–2.7 (2 H, m), 4.1–4.5 (1 H, pentet), 4.6–4.8 (1 H, sextet), 8.9–9.2 (1 H, s); **3** ^{13}C NMR ($CDCl_3$) δ 29.91, 36.21, 42.11, 47.65, 85.70.
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(18) Prepared from **5** by reaction with excess triphenylphosphine dibromide.
(19) **1** was found to inhibit arachidonic acid initiated human blood platelet aggregation at concentrations as low as 15 μM with I_{50} = 50 μM. We thank J. R. Nixon, J. H. Roycroft, and D. B. Menzel for conducting this study.

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[2 + 2] Photoaddition of Acetylenes to Hexafluorobenzene. Isolation of Bicyclo[4.2.0]octatriene Derivatives

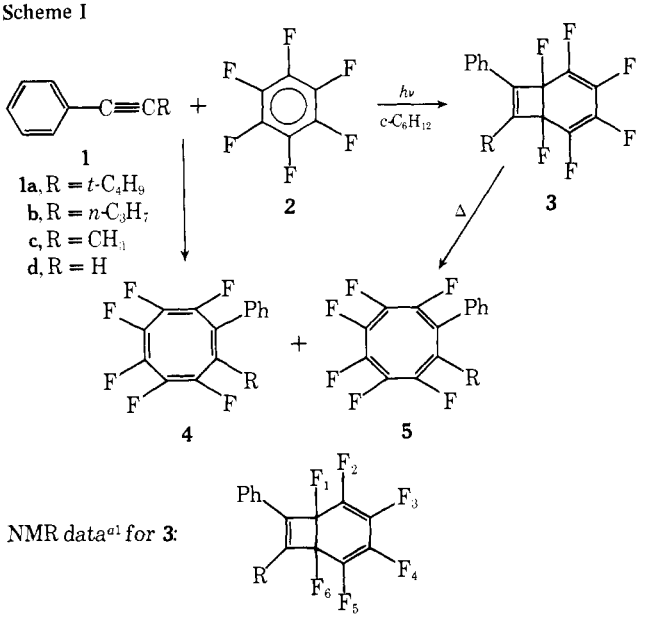
Sir:

Benzene and substituted benzenes undergo several types of cycloaddition reactions with olefins.[1] Photoaddition of acetylenes to benzene results in the formation of a cyclooctatetraene derivative via the bicyclo[4.2.0]octatriene derivative.[2] However, such an intermediate has never been isolated in photoaddition reactions. Recently, we have found that photoaddition of indene or 1,2-dihydronaphthalene to hexafluorobenzene results in the formation of cis-syn-cis[2 + 2] cycloadducts.[3] We now report that under photochemical conditions, hexafluorobenzene (**2**) readily reacts with phenyl-substituted acetylenes (**1**) to form the corresponding phenyl-substituted hexafluorobicyclo[4.2.0]octatrienes (**3**) in high yield.

A cyclohexane solution of 1-phenyl-2-*tert*-butylacetylene (**1a,** 10 mmol) and hexafluorobenzene (**2,** 20 mmol) was irradiated at 253.7 nm for 60 h. The structure of the product (**3a**) formed in high yield (86%) was established on the basis of its spectroscopic data. X-ray analysis[4] of **3c,** also formed in high yield, shows that a bicyclo[4.2.0]octatriene derivative was formed. The mass spectrum of **3a** shows the following major fragments: *m/e* 344 (M^+, 80%), 158 (82, phenyl-*tert*-butylacetylene species), 144 (41), 143 (100), 129 (55), 57 (64). A ^{19}F NMR spectrum of crude reaction mixture showed six multiplets and by careful measurement of pure product **3a** the following multiplets were observed: δF_2, δF_5 −151.1 ppm, −153.4 ppm as dddt; δF_1, δF_6 −154.9 ppm, −159.0 ppm as ddt, and δF_3, δF_4 −161.6 ppm, −162.75 ppm as tdd with coupling constants $^3J_{F_1,F_6}$ = 15 Hz, $^3J_{F_1,F_2}$ = $^3J_{F_5,F_6}$ = 35 Hz, $^3J_{F_2,F_3}$ = $^3J_{F_4,F_5}$ = $^4J_{F_2,F_4}$ = $^4J_{F_3,F_5}$ = 7 Hz, $^5J_{F_2,F_5}$ = 21 Hz, $^3J_{F_3,F_4}$ = 5 Hz, $^4J_{F_1,F_3}$ = $^4J_{F_4,F_6}$ = $^4J_{F_2,F_6}$ = $^4J_{F_1,F_5}$ = 1.5 Hz. The observed coupling constants are very similar to those, observed by fluorocyclopentadiene derivates.[5] It is very interesting, that fluorine atoms bonded at the sp^3 carbon atom appear at lower field than fluorine atoms at an sp^2 carbon atom. On heating (T = 150 °C), product **3a** was quantitatively transformed into product **5a,** which shows in its ^{19}F NMR spectrum five signals at lower field than those of **3a** (δF: −144 (m, 2F), −136.5 (d, 1F), −134.6 (d, 1F), −133.1 (dd, 1F), −130.1 (dd, 1F)). The mass spectrum shows the following major fragments: *m/e* 344 (M^+, 5%), 283 (35), 268 (33), 61 (37), 57 (100).

Being interested in the effect of the magnitude of the group R on the products formed in the photocycloaddition reaction, we found it instructive to study the reactions of acetylenes with *n*-propyl (**1b**), methyl (**1c**), and hydrogen (**1d**) as substituents. Acetylenes **1b** and **1c** gave products **3b** and **3c,** while in the case of **1d** a mixture of two products (**4d**:**5d** = 1.75:1) was formed. The mixture was separated by preparative GLC or TLC. Minor product **5d** shows in its ^{19}F NMR spectrum six signals (δF −123.75 (m), −125.25 (m), −127.5 (dd, J = 39 and 24 Hz), −129 (m), −135.75 (m)) and in its ^{1}H spectrum a doublet signal at 6.3 ppm (J = 24 Hz). Its mass spectrum shows the following major fragments: 288 (M^+, 100%), 273 (32), 219 (30), 120 (42), 102 (22). Major product **4d** shows in its ^{19}F NMR spectrum three signals at lower field than those of **5d**

Scheme I



NMR data[a] for **3**:

Compd	δF_3, δF_4	δF_1, δF_6	δF_2, δF_5	δR
3a	−162.75, −161.6	−159.0, −154.9	−153.4, −151.1	1.4
3b	−155.3	−152.6, −151.5	−148.1, −143.6	1.0, 1.8, 2.6
3c	−162, −160.5		−156.4, −150.4	2.1

[a] CCl_4 solvent, $CClF_3$ as internal standard.