Communications to the Editor

Peroxide Transfer from Tri-*n*-butyltin Peroxides. A Mild New Synthesis of Dialkyl Peroxides

Sir:

Prostaglandin (PG) endoperoxides[1] are a major synthetic challenge. They are thermally unstable, base sensitive, strained bicyclic peroxides. Mild, high yield methods for the synthesis of dialkyl peroxides are a key objective of our studies on the synthesis of PG endoperoxides.[2] We now report that the reaction of alkyl trifluoromethanesulfonates (triflates) with tri-*n*-butyltin peroxides[3] is a novel and effective new route to primary and secondary peroxides.

Primary and secondary dialkyl peroxides are generally prepared by base catalyzed alkylation of hydrogen peroxide with alkyl methanesulfonates. However, yields for secondary alkyl peroxides are particularly low.[7] We hypothesized that an alkyl triflate **1** would alkylate a bis(trialkyltin) peroxide **2** to yield an oxonium intermediate **3** (eq 1) in analogy with the

$$\underset{\mathbf{1}}{R'OTf} + \underset{\mathbf{2}}{R_3SnOOSnR_3} \longrightarrow \underset{\mathbf{3}}{R_3SnO(R')OOSnR_3}{}^{+}\ {}^{-}OTf \qquad (1)$$

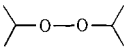
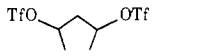
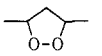
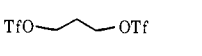
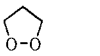
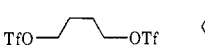
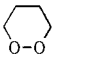
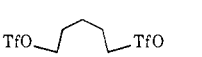
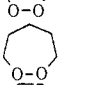
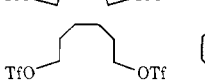
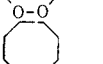
reaction of alkyl triflates with dialkyl ethers.[8] Expulsion of a relatively stable trialkyltin cation from **3** would give a trialkyltin alkyl peroxide **4.** A similar sequence would lead to a dialkyl peroxide **5** from **4** (eq 2).

$$\underset{\mathbf{4}}{R'OOSnR_3} \xrightarrow{R'OTf} \underset{}{R'O(R')OSnR_3}{}^{+}\ {}^{-}OTf \xrightarrow{-SnOTf} \underset{\mathbf{5}}{R'OOR'} \qquad (2)$$

In fact, alkyl triflates are consumed rapidly (10 min) at 20 °C upon exposure to bis(tri-*n*-butyltin) peroxide.[9] Dialkyl peroxides are obtained in exceptionally good yields (Table I) by simple distillation from the reaction mixture under reduced pressure. The corresponding dialkyl ethers are often produced in small though reproducible yields along with traces of 1-butanol. The peroxides are most conveniently purified by preparative gas-liquid phase chromatography.[10] In this manner we achieved the first syntheses of the five-, seven-, and eight-membered heterocycles 1,2-dioxolane, 1,2-dioxepane, and 1,2-dioxocane (table entries 3, 5, and 6). With the previously known 1,2-dioxane,[11] a homologous series of cyclic peroxides is now available. This series may be of some value for examining the effect of geometrical constraints on the properties of the O–O bond and the chemistry of dialkyl peroxides.

The following synthesis of diisopropyl peroxide is representative.[12] Bis(tri-*n*-butyltin) peroxide (1.0 mmol) and isopropyl triflate (2.2 mmol) were combined at room temperature in methylene chloride solution (2.5 mL) under nitrogen. After 10 min, the products and solvent were vacuum transferred at 20 mm into a cooled receiver (−78 °C) removing the last traces of product from the tin containing residue at 0.5 mm. ^{1}H NMR analysis ($CHCl_3$ standard) indicates diisopropyl peroxide (79%), isopropyl ether (7%), and traces of 1-butanol as the only volatile reaction products. Pure diisopropyl peroxide (52%) was obtained by preparative glc.[10] Previously, diisopropyl peroxide was obtained only under harsh alkaline conditions in 16–26% yield.[14]

Table I. Dialkyl Peroxides from Alkyl Triflates and Bis(tri-*n*-butyltin) Peroxide

Entry	Starting triflate	Peroxide	Yield (%)	Ether yield (%)
1			79	7
2			52	—
3			68	0
4			65	24
5			37	42
6			23	6

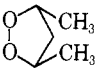
Though further study is necessary to establish a mechanism, it is tempting to speculate that formation of the by-product ethers and butanol involves alkylation of **4** β to tin to give **6** which in turn decomposes with butyl migration to oxygen (eq 3). As predicted by the mechanism of eq 2, treatment of *tert*-

$$\underset{\mathbf{4}}{R'OOSnBu_3} \xrightarrow{R'OTf} \underset{\mathbf{6}}{R'O(R')O(Bu)SnBu_2}{}^{+}\ {}^{-}OTf \longrightarrow R'OR' + (BuOSnBu_2)OTf \qquad (3)$$

butyl tri(*n*-butyl)tin peroxide with isopropyl triflate gives *tert*-butyl isopropyl peroxide (79%).

An ether by-product, oxetane, was not observed in the synthesis of 1,2-dioxolane (table entry 3). This is important since there is a 1,2-dioxolane ring in the 2,3-dioxabicyclo[2.2.1] heptane nucleus (**7**) of PG-endoperoxides. Moreover, the bis-secondary peroxide, 3,5-dimethyl-1,2-dioxolane (**8**),[15] is

7



8

formed in good yield (table entry 2).[16] Nevertheless, this mild new method for the synthesis of dialkyl peroxides fails to give **7** when applied to 1,3-cyclopentyl ditriflate. However, a modified procedure which does provide the reactive peroxide **7** is described in the accompanying communication.

Acknowledgment. This work was supported by Grant GM-21249 from the Division of General Medical Sciences of the National Institutes of Health. We thank A. J. Bloodworth for a ^{1}H NMR spectrum of 3,5-dimethyl-1,2-dioxolane.

References and Notes

(1) (a) P. F. Beal, G. S. Fonken, and J. E. Pike, Belgium Patent 659 984 (1964); (b) B. Samuelsson, *J. Am. Chem. Soc.*, **87**, 3011 (1965); (c) M. Hamberg and B. Samuelsson, *ibid.*, **88**, 2349 (1966); (d) *J. Biol. Chem.*, **242**, 5329, 5336, 5344 (1967); (e) B. Samuelsson, *Prog. Biochem. Pharmacol.*, **3**, 59 (1967); (f) *ibid.*, **5**, 109 (1969); (g) *Fed. Proc., Fed. Am. Soc. Exp. Biol.*, **31**, 1442 (1972); (h) M. Hamberg and B. Samuelsson, *Proc. Natl. Acad. Sci. U.S.A.*, **70**, 899 (1973); (i) D. H. Nugteren and E. Hazelhof, *Biochim. Bio-*

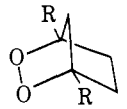
phys. Acta, **326**, 448 (1973); (j) C. Pace-Asciak and M. Nashat, *ibid.*, **388**, 243 (1975).
(2) (a) R. G. Salomon and R. D. Gleim, *J. Org. Chem.*, **41**, 1529 (1976); (b) M. F. Salomon, R. G. Salomon, and R. D. Gleim, *ibid.*, **41**, 3983 (1976); (c) D. J. Coughlin and R. G. Salomon, *J. Am. Chem. Soc.*, **99**, 655 (1977).
(3) Trialkyltin peroxides are easily prepared by reaction of trialkyltin methoxide[4] with either alkyl hydroperoxides, to produce trialkyltin alkyl peroxides,[5] or with anhydrous hydrogen peroxide[6] to produce bis(trialkyltin) peroxides.[5]
(4) D. L. Alleston and A. G. Davies, *J. Chem. Soc.*, 2050 (1962).
(5) A. Rieche and J. Dahlmann, *Justus Liebigs Ann. Chem.*, **675**, 19 (1964).
(6) F. D. Greene and J. Kazan, *J. Org. Chem.*, **28**, 2168 (1963).
(7) R. Hiatt, *Org. Peroxides*, **3**, 6 (1972).
(8) (a) T. Gramstad and R. N. Haszeldine, *J. Chem. Soc.*, 4069 (1957); (b) H. A. Brown, Abstracts, 128th National Meeting of the American Chemical Society, Minneapolis, Minn., April 1955, 29M.
(9) Tri(*n*-butyl)tin methoxide[4] (40 mmol) is added dropwise over 3 min to 1 M anhydrous hydrogen peroxide (20 mmol) in ethyl ether[6] at 0 °C under a blanket of dry nitrogen. After stirring 2 h at 0 °C, solvent and methanol are removed at 20 mm, the last traces being removed at 0.5 mm. Bis(trialkyltin) peroxides are somewhat unstable, but bis(tri-*n*-butyltin) peroxide may be stored under nitrogen without appreciable decomposition for several weeks in anhydrous methylene chloride solution at −20 °C. *CAUTION:* all reactions involving peroxides and especially anhydrous hydrogen peroxide should be performed behind a safety shield.
(10) A short column filled with 10% Dow Corning 710 silicone on 60/80 mesh acid washed-DMCS treated Chromosorb W. Diisopropyl peroxide,[14] 3,5-dimethyl-1,2-dioxolane,[15] and 1,2-dioxane[11] were identified by spectral comparison with authentic samples. Approximately equal amounts of the cis and trans isomers of 3,5-dimethyl-1,2-dioxolane were obtained. New compounds were characterized by elemental analysis and spectra: *1,2-dioxolane* ^{1}H NMR (CCl_4) δ 3.92 (4 H, t, J = 7 Hz), 2.53 (2 H, quint, J = 7 Hz); IR (neat) 1150 (s), 1110 (s), 987 (m), 925 (m), 780 (w); mass spectrum *m/e* (rel intensity) 26 (28), 27 (48), 28 (64), 29 (100), 30 (25), 31 (39), 42 (41), 43 (47), 44 (26), 46 (20), 74 (44); *1,2-dioxepane* ^{1}H NMR (CCl_4) δ 4.00 (4 H, m), 1.80 (6 H, m); IR (neat) 1443 (s), 1360 (m), 1260 (m), 1130 (m), 1060 (s), 1000 (s), 977 (m), 918 (m), 863 (m), 791 (m); mass spectrum *m/e* (rel intensity) 27 (79), 28 (89), 29 (94), 31 (42), 39 (62), 41 (100), 42 (69), 43 (60), 44 (40), 55 (67), 56 (69), 102 (50); *1,2-dioxocane* ^{1}H NMR (CCl_4) δ 3.87 (4 H, m), 1.70 (8 H, m); IR (neat) 1445 (s), 1370 (m), 1190 (m), 1150 (m), 1105 (m), 1070 (s), 1020 (s), 1005 (s), 947 (s), 845 (w), 816 (w), 770 (w), 733 (w); mass spectrum *m/e* (rel intensity) 27 (69), 28 (63); 29 (100), 31 (57), 39 (59), 41 (95), 42 (59), 43 (51), 44 (40), 55 (68), 56 (23), 57 (51), 67 (37), 68 (35), 69 (32), 70 (45), 98 (20), 116 (27).
(11) R. Criegee and G. Muller, *Chem. Ber.*, **89**, 238 (1956).
(12) Bis(triethylgermyl) peroxide[5] is less reactive (3 h for completion) and gives diisopropyl peroxide (41%) and isopropyl ether (9%). Bis-(trimethylsilyl) peroxide[13] gives no diisopropyl peroxide even after exposure to isopropyl triflate for 1 week at 20 °C.
(13) A. Simon and H. Arnold, *J. Prakt. Chem.*, **8**, 241 (1959).
(14) W. A. Pryor, D. M. Huston, T. R. Fiske, T. L. Pickering, and E. Ciuffarin, *J. Am. Chem. Soc.*, **86**, 4237 (1964).
(15) A. J. Bloodworth and M. E. Loveitt, *J. Chem. Soc., Chem. Commun.*, 94 (1976).
(16) For other synthesis of 3,5-dialkyl-1,2-dioxolanes see (a) P. M. Jacobs and A. H. Soloway, *J. Org. Chem.*, **39**, 3427 (1974); (b) E. J. Corey, K. C. Nicolaou, M. Shibasaki, Y. Machida, and C. S. Shiner, *Tetrahedron Lett.*, 3183 (1975); (c) N. A. Porter, M. O. Funk, D. Gilmore, R. Isaac, and J. Nixon, *J. Am. Chem. Soc.*, **98**, 6000 (1976); (d) N. A. Porter and D. W. Gilmore, *ibid.*, **99**, 3503 (1977).

Mary F. Salomon,* Robert G. Salomon*
Department of Chemistry, Case Western Reserve University
Cleveland, Ohio 44106
Received November 15, 1976

2,3-Dioxabicyclo[2.2.1]heptane. The Strained Bicyclic Peroxide Nucleus of Prostaglandin Endoperoxides

Sir:

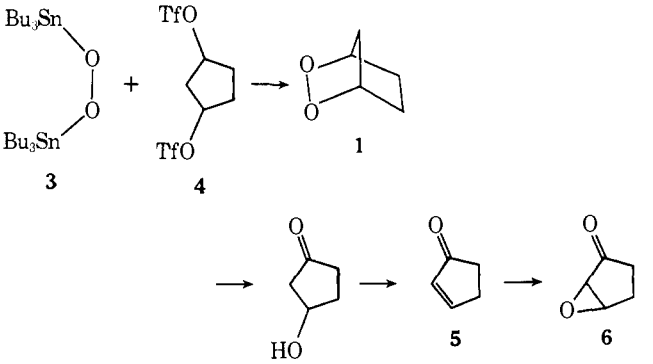
The 2,3-dioxabicyclo[2.2.1]heptane (**1**) heterobicyclic ring system assumed special importance when it was recognized as the nucleus of prostaglandin (PG) endoperoxides,[1] the pivotal immediate biological precursors of prostaglandins,[2] thromboxanes,[3] and prostacyclins.[4] We now report the first synthesis of the parent compound **1**, and record some preliminary observations on the chemical and thermal reactions of this important molecular type.



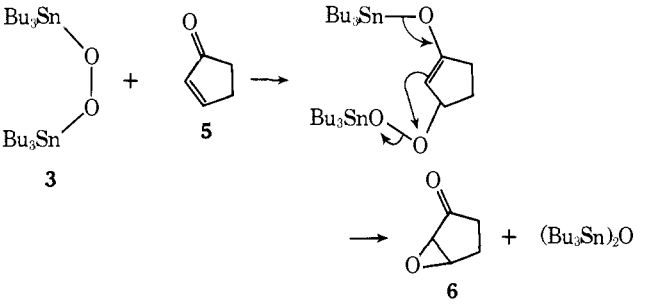
1, R = H
2, R = C_6H_5

Recently, we described the first nonenzymatic synthesis of fully characterized derivatives of **1**.[5] The bridgehead substitution in the 1,4-diphenyl derivative **2** precluded PG-endoperoxide-like reactivity involving abstraction of a bridgehead proton. The stability of **2** was found not to differ significantly from common ditertiary alkyl peroxides in contrast with the extreme thermal and chemical instability observed for PG-endoperoxides.[11] In planning a synthesis of **1**, we assumed that this bridgehead unsubstituted bis secondary alkyl peroxide would be especially sensitive toward base induced disproportionation[6] as observed for PG-endoperoxides. Our previous discovery that alkyl hydroperoxides can be alkylated in excellent yields with secondary alkyl trifluoromethane sulfonates (triflates) under mild, nonalkaline conditions,[7] led us to examine the reaction of bis(tri-*n*-butyltin) peroxide (**3**) with alkyl triflates. The successful development of an effective new synthesis of primary and secondary peroxides based on peroxide transfer from **3** to alkyl triflates was described in the accompanying communication.

A bistriflate **4** was prepared from *cis*-1,3-cyclopentanediol as described previously.[7] An exothermic reaction occurred when **3** and **4** were combined in a 1:1 molar ratio. No trace of **1** was detected in the reaction product mixture by ^{1}H NMR. The volatile products, isolated by vacuum transfer (0.03 mm) into a cold trap (−78 °C), included variable amounts of 2-cyclopenten-1-one (**5**)[8] and 2,3-epoxycyclopentan-1-one (**6**).[9]



It seemed likely that **5** arose by disproportionation of the sensitive peroxide **1** under the reaction conditions, followed by dehydration of the resulting β-hydroxy ketone, as in the disproportionation of PG-endoperoxides to PGE and subsequent dehydration to PGA. Apparently, as expected, the rigid, strained, bicyclic peroxide **1** is unusually reactive. The α,β-unsaturated ketone **5** was shown to give **6** (40% yield) upon treatment with **3**. This novel aprotic epoxidation most likely involves initial nucleophilic 1,4-addition to eneone **5**, followed by intramolecular nucleophilic displacement of tin oxide.[10]



Since **3** is essentially nonvolatile, alkylations of **3** can be conducted in vacuo, in contrast with syntheses of peroxides based on alkylation of hydrogen peroxide. The bicyclic peroxide **1** was obtained in 13% yield, when the reaction between **3** and **4** was conducted in vacuo (0.1 mm) with transfer of the volatile products to a cold trap (−78 °C) as they were formed. Best results were achieved with 1,2,4-trichlorobenzene as re-