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INTRAMOLECULAR ALKYLATION OF PEROXIDES AND HYDROPEROXIDES; PEROXIDE TRANSFER VIA PEROXONIUM INTERMEDIATES

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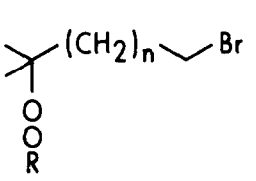
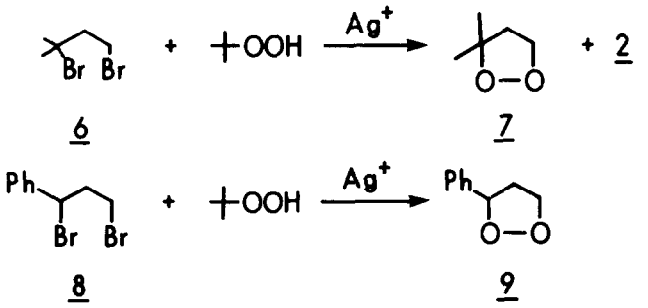
Abstract: A series of homologous peroxy-bromides is reacted with silver ion in organic solvents. Cyclic peroxide formation occurs along with peroxide transfer to the carbon originally bearing bromine. A preference for five-membered ring peroxonium ion formation is observed in these intramolecular alkylations.

The chemistry of β-bromohydroperoxides, 1, has been the focus of considerable interest in the past ten to fifteen years.(1,2) As precursors to dioxetanes, these hydroperoxides have played a prominent role in the development of theories of chemiluminescence and singlet oxygen reactivity. In the course of our studies on the chemistry of cyclic peroxides,(3) we have investigated the chemistry of peroxy-bromide homologs of 1. We report here on the novel chemistry of the silver ion assisted reactions of the bromo-peroxides 2-5.(4,5)



1; R = H, n = 0
2; R = t-butyl, n = 1
3; R = t-butyl, n = 2
4; R = t-butyl, n = 3
5; R = H, n = 2

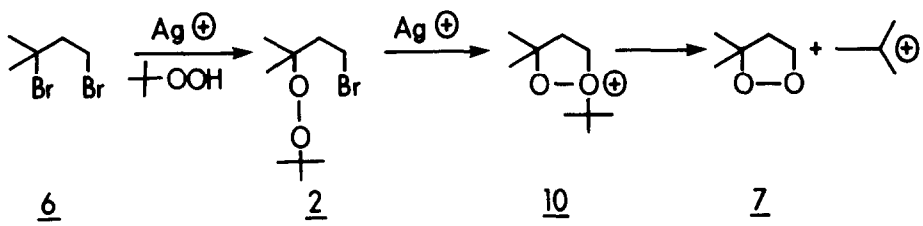
Our interest in the chemistry of these bromoperoxides was stimulated by the unanticipated reaction of the dibromide 6 and 8 with t-butyl hydroperoxide to give the cyclic peroxides 7 and 9.(4)



When one equivalent of dibromide 6 or 8 is combined with three equivalents of t-butyl hydroperoxide and two equivalents of either silver tetrafluoroborate or silver trifluoroacetate in pentane at room temperature, dioxolane 9 is isolated in over 50% yield from 8. Similar reaction of 6 affords 7 (30%) along with the bromoperoxide 2 in 11-18% isolated yield. Reaction of these dibromides with t-butyl hydroperoxide (90%) offers a safer and more convenient route to the resultant cyclic peroxides than analogous reaction with hydrogen peroxide (90%). Yields of dioxolanes 7 and 9 were however, 10-15% lower when utilizing this alkyl hydroperoxide than with hydrogen peroxide. The isolation of 2 along with 7 suggests that this bromo-peroxide may be an intermediate in the conversion of 6 → 7 and the following experiments support this view.

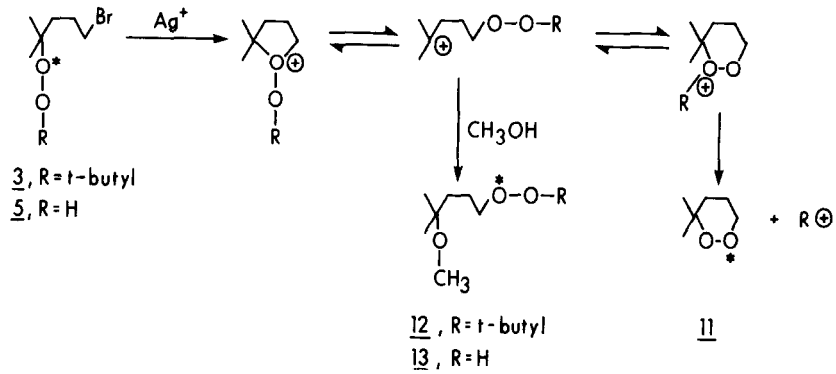
Reaction of 2 in methylene chloride at 0°C with 1.1 equivalents silver trifluoroacetate or silver tetrafluoroborate results in quantitative conversion of 2 to 7. The reaction is rapid at 0°C and occurs at temperatures below -50°C. The bromoperoxide 2 reacts with silver salts in methanol solvent to give 7 plus t-butyl methyl ether in high yield. The conversion of 6 to 7 may thus be best explained by a mechanism as outlined in Scheme 1. This mechanism involves the unprecedented intramolecular alkylation of a dialkyl peroxide with formation of an intermediate peroxonium ion 10.

Scheme 1



Peroxy-bromide 3 is converted to the cyclic peroxide 3,3-dimethyl-1,2-dioxane, 11(4), (70% yield) when treated with silver tetrafluoroborate in methylene chloride. Reaction of 3 with silver ion in methanol solvent, however, reveals a significant difference in the course of the silver induced reactions of peroxy-bromides 2 and 3. While 2 gave the cyclic peroxide 7 in either methanol or methylene chloride solvent (vide supra), 3 gives no detectable cyclic peroxide in methanol. Instead, reaction of 3 with silver ion in methanol yields the peroxy-transfer product 12(4) in 40% isolated yield (HPLC). A mechanism that accounts for the product-solvent dependence is presented in Scheme 2.

Scheme 2

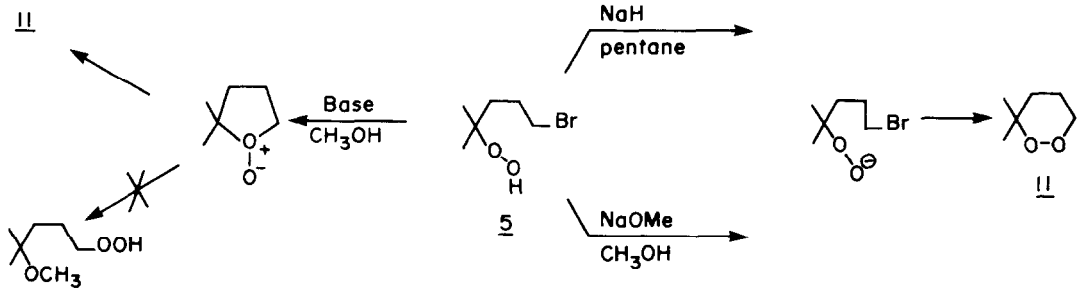


Again, intramolecular peroxide alkylation is proposed to account for products 11 and 12. Formation of 12 in methanol solvent suggests that the intramolecular alkylation preferentially occurs to give a five-membered ring peroxonium ion rather than the six-membered ring species.(6)

A mechanistic scheme similar to that written for 3 may also be written for the reaction of bromo-hydroperoxide 5 with silver ion. Thus in methylene chloride with silver ion, 5 gives the 1,2-dioxane 11 while in methanol the major isolated product is the peroxy-transfer product 13. We note that the peroxy-transfer mechanism requires an oxygen-oxygen interchange in the conversion of 3 or 5 to 11. That is, oxygen adjacent to the tertiary alkyl bromide center in 3 or 5 ends up substituted to the primary carbon in the cyclic peroxide product 11 as indicated by (*) in Scheme 2.

When hydroperoxide 5 is reacted with base in either nucleophilic or nonnucleophilic solvent however, no peroxy-transfer products are recovered. Instead, conversion to cyclic peroxide occurs in good yield.

Scheme 3



If 5 is reacted with sodium hydride in pentane, dioxane 11 is produced in 43% yields. Also, if hydroperoxybromide 5 is reacted with sodium methoxide in methanol, dioxane 11 is produced in 52% yield with no indication of solvent trapping products. These reaction products would

indicate that upon reaction of this 1,4-hydroperoxybromide with base, attack is made to displace bromide by the outside anionic oxygen thus forming the six membered ring dioxane 11. An alternate route we have no data to support is the formation of the kinetic five membered ring peroxonium, followed by rapid peroxy-transfer and subsequent ring closure as detailed in Scheme 3.

Peroxide 4 is much less reactive with silver ion than is 2 or 3. Reaction of 4 with silver tetrafluoroborate does occur in refluxing methanol and leads to the simple solvolysis product of the primary bromide. The peroxide functional group is apparently not involved in this simple solvolysis. The studies outlined here indicate that peroxonium intermediates may be formed by intramolecular alkylation of dialkyl peroxides or alkyl hydroperoxides. Trialkylperoxonium salts such as those proposed as intermediates from 2 and 3 are previously unreported and the alkylation procedure outlined here appears to provide a straightforward route to these species. The chemistry of such peroxonium intermediates is currently being explored in our laboratories.

References and Notes

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5. Structure supported by elemental analysis.
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