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MERCURY(II)-MEDIATED CYCLISATION OF HYDROPEROXYALKYLCYCLOPROPANES: A NEW ROUTE TO CYCLIC PEROXIDES

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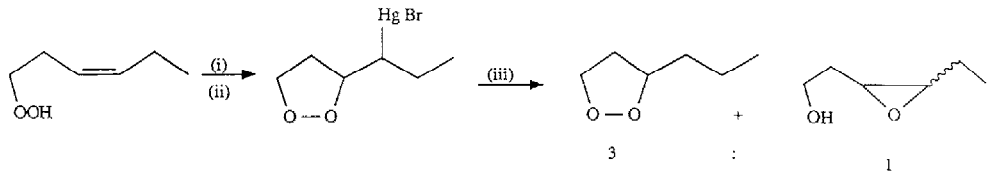
Summary: Aldehydes, RCHO (R = Me, Et, ^{i}Pr, and c-C_6H_{11}), have been converted via alkylation, cyclopropanation, oxidation, condensation with *p*-tosylhydrazine, reduction and perhydrolysis into 2-hydroperoxyalkylcyclopropanes, $RCH(OOH)CH_2c\text{-}C_3H_5$, and thence by cycloperoxymercuriation and reductive demercuriation into the corresponding 3-alkyl-5-ethyl-1,2-dioxolanes.

Mercury(II)-mediated cyclisation of alkenyl hydroperoxides provides the basis of a useful synthetic route to cyclic peroxides.[1-6] The mercury substituent in the cyclisation product can usually be replaced by hydrogen by reaction with alkaline sodium borohydride, thereby completing a two-step conversion of alkenyl hydroperoxide into the isomeric cyclic peroxide corresponding to O-H addition across the double bond (*eg*[1] scheme 1)



Scheme 1 *Reagents*: (i) $Hg(NO_3)_2.H_2O$, CH_2Cl_2 (ii) KBr, H_2O (iii) $NaBH_4$, NaOH.

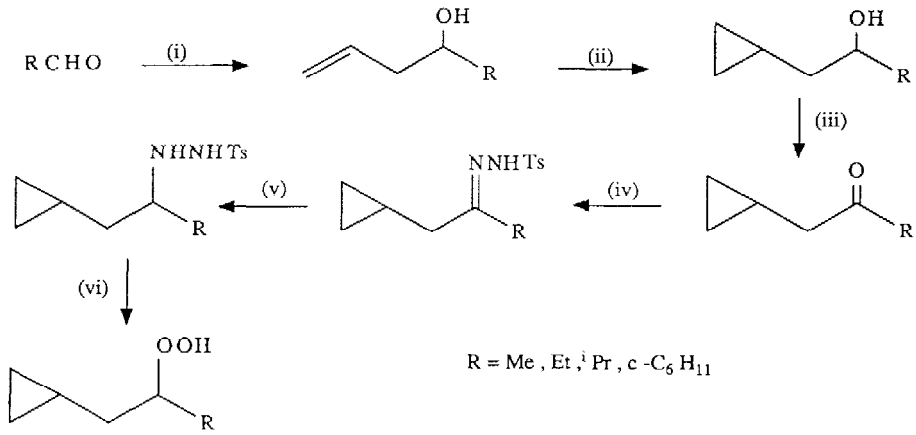
However, the demercuriation proceeds by a free radical mechanism and the *β*-peroxyalkyl radical partitions between hydrogen abstraction to give the desired cyclic peroxide and intramolecular homolytic displacement at oxygen to afford, after subsequent hydrogen abstraction, an hydroxyalkyloxirane (*eg*[1] scheme 1). The extent of hydroxyalkyloxirane formation depends crucially upon the structure of the cyclic peroxide[7] and can become predominant.[1-3] Clearly the

availability of this competing pathway in the reduction step detracts from the generality and value of this method of preparing cyclic peroxides.

The peroxymercuriation of cyclopropanes affords peroxides with the mercurio substituent one carbon atom further removed from the O-O bond than in those derived from alkenes. The rather limited data available[8-10] indicate that these compounds undergo reductive demercuriation without the complication of competing intramolecular homolytic substitution at oxygen. Although the cleavage of γ-peroxyalkyl radicals to oxetanes has been observed under other conditions[11], it appears to be too slow to compete effectively with hydrogen abstraction during demercuriation.

The aim of this work was to examine the hitherto unknown process of intramolecular peroxymercuriation of cyclopropanes as an alternative route to cyclic peroxides to see if the potential advantage of a cleaner reductive demercuriation could be realised.

Previous examples of other types of intramolecular oxymercuriation of cyclopropanes are rare, but the reported isolation of lactone and tetrahydrofuran derivatives[12] provided an encouraging precedent. Examples of hydroperoxyalkylcyclopropanes are also rare and none of the reported compounds[13-15] appeared promising as a candidate for mercury(II)-mediated cyclisation. Accordingly, the first step was to develop a viable and preferably general synthesis of suitable hydroperoxyalkylcyclopropanes. The route finally adopted is shown in scheme 2.

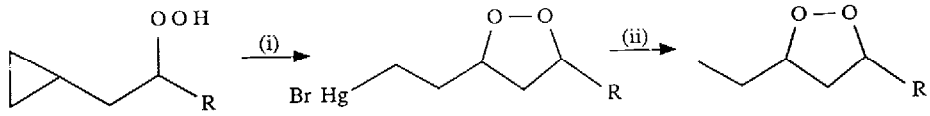


Scheme 2 *Reagents*: (i) CH_2=CH-CH_2MgBr then H_3O^+ (ii) CH_2I_2, Zn/Cu (iii) PCC (iv) $TsNHNH_2$ (v) $py.BH_3$ (vi) H_2O_2, Na_2O_2.

The cyclopropane group is introduced early in the sequence by a Simmons-Smith reaction. The method of then transforming hydroxyl into hydroperoxyl is basically the same as that used by us to prepare alkenyl hydroperoxides.[5] Once again it gives far better yields than the conventional route involving perhydrolysis of mesylates. A key modification was the replacement of sodium cyanoborohydride by pyridine-borane[16] for the reduction of the *p*-tosylhydrazones. This provided a much cleaner product in addition to being experimentally more convenient.

By optimising conditions for each example, yields of 72-98% were achieved in each step except for the perhydrolysis where only 42-52% could be managed when R ≠ Me. The hydroperoxides were purified by chromatography on silica at 0 °C. It should be noted that two examples with aromatic aldehydes (R = Ph, 4-$MeOC_6H_4$) proceeded satisfactorily to the *N*-alkyl-*N'*-*p*-tosylhydrazine stage but then failed to yield any hydroperoxide.

Cycloperoxymercuriation (scheme 3) did not proceed with mercury(II) acetate alone and required perchloric acid catalysis as in the analogous intermolecular reactions.[9,10,17] However, the reactions were much cleaner than the intermolecular ones and recrystallisation of the crude product gave each bromomercurioethyl-1,2-dioxolane[18] in a yield of over 80%. Each product was obtained as a mixture of *cis* and *trans* isomers in a ratio of about 60:40.



R = Me , Et , ^{i}Pr , c - C_6H_{11}

Scheme 3 *Reagents*: (i) $Hg(OAc)_2$, 0.2 $HClO_4$, CH_2Cl_2 (ii) KBr, H_2O (iii) $NaBH_4$, NaOH.

Reduction with alkaline sodium borohydride (scheme 3) afforded the corresponding 3-alkyl-5-ethyl-1,2-dioxolanes[18] which after purification by chromatography on silica at O °C were isolated in yields of 52-60%. In each case by-products, which are as yet unidentified, were formed but amounted to less than 10% of the product mixture.

The nearest analogous reduction of an alkenyl hydroperoxide-derived peroxymercurial is that shown in scheme 1 where the by-product amounted to 25% of the product mixture.[1] It therefore appears likely that the new route does possess the expected advantage. However, more work is

needed to establish this firmly, especially in the challenging field of 1,2-dioxane synthesis where the alkenyl hydroperoxide route appears to be markedly less successful.[1-3]

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18. Each 1,2 dioxolane gave a positive peroxide test with acidified ferrous thiocyanate, had consistent ^{1}H and ^{13}C NMR spectra, and gave correct elemental analysis and/or correct accurate mass for the molecular ion in the electron impact (70 ev) mass spectrum.

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