Photo-oxygenation of Indene and 1,2-Dihydronaphthalene: Formation of 1,2-Dioxetanes and 1,2,4-Trioxanes

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Abstract. The methylene blue (MB)-sensitized photo-oxygenation of indene (1) in CH₂OH gave trans-2-hydroperoxy-1-methoxyindane (9), homophthalaldehyde (4), and its cyclic acetal 8. The same reaction conducted in acetaldehyde gave only 4. Repetition of the photo-oxygenation of 1 in slightly acidic aq. acetone (1:9) gave essentially trans-2-hydroperoxy-1-hydroxyindane (14) together with some cis-5,6-dihydro-3,3-dimethyl-1,2,4-trioxinol[1,2-e]indene. The MB-sensitized photo-oxygenation of 1,2-dihydronaphthalene (16) in CH₃OH gave 1,4-dihydro-1-hydroperoxy-naphthalene (17) and trans-1,2,3,4-tetrahydro-2-hydroperoxy-1-methoxynaphthalene (19). In acetaldehyde, 16 furnished only 17. In aq. acetone (1:9) 16 gave 17 and trans-2-hydroperoxy-1-hydroxy-1,2,3,4-tetrahydronaphthalene (23). Product compositions were rationalized in terms of the 2-peroxides of the 1-cation of 1 and 16, namely 11 and 20. Treatment of 23 with aldehydes and ketones on catalysis with Amberlyst-15 or trimethylsilyl trifluoromethanesulfonate afforded the trans-fused 1,2,4-trioxanes 25. The 1,2-dioxetanes of 1 and 16 condensed with acetaldehyde on catalysis with CF₃COOH to give the cis-fused 1,2,4-trioxanes 12 and 22.

Introduction

The dye-sensitized photo-oxygenation of olefins constitutes an important chapter in organic chemistry [1]. Depending on the olefin, reaction can occur to give hydroperoxides, 1,2-dioxetanes, and endoperoxides. These oxygenated products are of obvious synthetic value, but the manner of their formation is also important and has commanded considerable attention over the years. As a molecule for testing mechanism, indene (1) has been much studied, since its structure allows it to undergo all three of the above-mentioned reaction courses.

The first photo-oxygenation of 1 was carried out in 1968, and innocuously enough was the start of a long polemic on the nature of the primary intermediates [2]. In CH₂Cl₂, a single product, homophthalaldehyde 4, was obtained which was thought to arise from the hydroperoxide 2.

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naphthalene (16) and two derivatives 26 and 27 which resemble 1. The photo-oxygenation of 1 was sensitized by methylene blue (MB) in CH$_3$OH and performed for 10 h at 10°C. Three products were isolated, trans-2-hydroperoxy-1-methoxyindane (9, 35%), homophthalaldehyde (4, 20%), and the cyclic acetal (8, 36%) (Scheme 3).

This result indicates that a molecule of singlet oxygen has added to 1 to form the zwitterionic species 11 which enjoys stabilization as a benzylic cation. Closure to dioxetane 5 soon follows. Cleavage together with methanolysis accounts for 4 and 8. Significantly, 11 lives long enough to undergo external capture by a molecule of CH$_3$OH. The peroxide group first acquires a proton to give the cation 6 which is then attacked on its least hindered side by CH$_3$OH so producing 9. The resulting trans-product does not equilibrate with the cis-isomer 10 owing to the poor nucleofugacity of the CH$_3$O group.

Repertition of the photo-oxygenation in a ten-fold excess of acetaldehyde several times at temperatures between -78°C and 20°C.

Scheme 4

5

Scheme 5

for mechanistic studies. RB possesses the additional property of being able to reduce singlet oxygen to superoxide radical anion [6]. Decomposition of the latter to H$_2$O$_2$ then results in the epoxidation of susceptible olefins such as adamantylidene-adamantane. Some of the aforementioned products could have arisen from the action of superoxide radical anion or H$_2$O$_2$ on 1.

Other evidence obtained from the photo-oxygenation of 1,3-dimethylindole [7] and 2-methoxy-norbornene [8] suggests that singlet oxygen reacts with electron-rich double bonds to form zwitterionic peroxides as the first event. Indene (1) should behave similarly. By a suitable choice of solvent, namely CH$_3$OH or acetaldehyde, the identity of the relevant ionic peroxides could be revealed.

Results and Discussion

We now report on such trapping experiments which have been carried out on 1 and for good measure on 1,2-dihydro-indene (16) and two derivatives 26 and 27 which resemble 1. The photo-oxygenation of 1 was sensitized by methylene blue (MB) in CH$_3$OH and performed for 10 h at 10°C. Three products were isolated, trans-2-hydroperoxy-1-methoxyindane (9, 35%), homophthalaldehyde (4, 20%), and the cyclic acetal (8, 36%) (Scheme 3). This result indicates that a molecule of singlet oxygen has added to 1 to form the zwitterionic species 11 which enjoys stabilization as a benzylic cation. Closure to dioxetane 5 soon follows. Cleavage together with methanolysis accounts for 4 and 8. Significantly, 11 lives long enough to undergo external capture by a molecule of CH$_3$OH. The peroxide group first acquires a proton to give the cation 6 which is then attacked on its least hindered side by CH$_3$OH so producing 9. The resulting trans-product does not equilibrate with the cis-isomer 10 owing to the poor nucleofugacity of the CH$_3$O group.

Repertition of the photo-oxygenation in a ten-fold excess of acetaldehyde several times at temperatures between -78°C and 20°C.
general, such hydroperoxy cations readily condense with carbonyl partners to afford cis-fused 1,2,4-trioxanes [10].

1,2-Dihydronaphthalene (16) has a structure which is similar to that of indene (1), but its photo-oxygenation has been studied less [11]. The products obtained in the RB-sensitized experiment [12] in acetone at −78° were just the 1-hydroperoxy derivative 17 (23%) and the adduct of a double addition of oxygen (18, 67%) (Scheme 6). Re-examination of this reaction at 10° in CH₂OH by using MB as sensitizer gave a result reminiscent of that found with indene (1). The hydroperoxide 17 (66%) was obtained as before, but accompanied by trans-1,2,3,4-tetrahydro-2-hydroperoxy-1-methoxynaphthalene (19, 30%) (Scheme 6). Again, the presence of 19 can be attributed to the primary peroxidic zwitterion 20 which has successfully captured a proton and CH₂OH to give successively 21 and 19. As before, 20 could not be intercepted to give trioxane 22, even when the photo-oxygenation of 16 was conducted in an overwhelming excess of acetaldehyde (Scheme 6). Evidently, 20 and 11 are equally inert towards aldehydes. An essential difference between 1 and 16 is that the ene-type reaction operates for the latter as a competing mode.

In an aq. medium, acetone/H₂O 9:1 with or without a drop of HCl, 16 reacted with singlet oxygen to give the usual ene product 17 (60%) and the trans-hydroperoxy alcohol 23 (29%) (Scheme 7). No trace of 1,2,4-trioxane 24 was detected.

20° gave none of the expected 1,2,4-trioxane 12, but only 4 (Scheme 4). Clearly, the intermediate 11 is either not reactive enough or too short-lived to be intercepted by a molecule of acetaldehyde. However, when the above experiment was carried out in aq. acetone (1:9) containing traces of HCl, trans-2-hydroperoxy-1-hydroxyindane (14) became the main product (72%) (Scheme 5). A tiny amount of the chloro analogue 13 (2%) and the cis-fused 3,3-dimethyl-1,2,4-trioxane 15 (7%) were also obtained. The configurations of 14 and 15 were ascertained by their reduction with NaBH₄ and LiAlH₄, resp., to the known trans- and cis-1,2-indane diols [9].

The origin of 15 was not the trans-hydroperoxy alcohol 14, since it did not react with acetone on catalysis with Amberlyst-15 or CuSO₄. The trans-methoxy hydroperoxide 9 was equally inert. Obviously, the dipolar species 11 is inert towards acetone as it did not even react with the more electrophilic acetaldehyde molecule. A reasonable candidate is the hydroperoxybenzyl cation 6 which is in equilibrium with the chloro derivative 13. In

Scheme 6

Scheme 7

Scheme 8
Varying the amount of HCl had no effect on the product composition.

The failure to isolate trioxane prompted further tests on 19 and 23. Like 9, 19 proved unreactive to acetaldehyde on catalysis with Amberlyst-15 or trimethylsilyl trifluoromethanesulfonate (TMSOTf) (Scheme 8). On the other hand, unlike trans-2-hydroperoxy-1-hydroxyindane (14), 23 underwent efficient condensation with both aldehydes and ketones (R1R2CO) on catalysis with Amberlyst-15 to give the corresponding trans fused 1,2,4-trioxanes (25) in high yield. Several of these compounds were stable, crystalline solids which permitted their structures to be determined by X-ray analysis [13]. The trioxane obtained from acetone (25a, R1=R2=Me) revealed that the fusion of the new oxygenated ring is trans, and that the ring itself adopts a chair conformation (Fig.). This result is of synthetic utility as most bicyclic 1,2,4-trioxanes prepared so far are cis-fused.

Lastly, the effect of substituents on the course of the photo-oxygenation of 16 was assayed. The 6-nitro derivative 26 proved to be totally unreactive which undeniably is due to the lowering of the energy of the HOMO of the styrene-like part of the molecule (Scheme 9). Conversely, the 6-methoxy derivative 27 in acetone/H2O (9:1) as solvent underwent complete reaction within 1 h to deliver the dialdehyde 29 (81%) and its cyclization product 30 (10%). No sign of the 2-hydroperoxy-1-hydroxy derivative analogous to 23 was seen. Obviously, a capturable, discrete zwitterionic peroxide is not formed; therefore, formation of the dioxetane 28 from 27 is likely to be concerted.

A final set of experiments was performed with authentic samples of the 1,2-dioxetanes of indene (5) [15] and 1,2-dihydronaphthalene (31) [16] to rule out the possibility that they were intermediates rather than the zwitterionic species (Scheme 10). Both were inert to neutral CH3OH, however, on catalysis with CF3COOH both underwent ready condensation with acetaldehyde in CH2Cl2 to afford the cis fused 1,2,4-trioxanes (12 and 22) in yields of 95 and 75%, resp.

**Conclusion**

The present results attest to the formation of zwitterionic peroxides 11 and 20, when singlet oxygen collides with indene (1) and 1,2-dihydronaphthalene (16). The positive charge in 11 and 20 is stabilized as a benzylic cation, whereas the negative charge exists simply as the free peroxide ion. The latter is easily protonated, but is unable to add to the aldehyde function. In CH3OH, some of 11 escapes capture and closes to dioxetane 5. In contrast, 20 is completely captured by CH2OH. Furthermore, 16 undergoes hydroperoxidation as a second course of reaction.

Both olefins 1 and 16 are different from 2-methoxy norbornene and 2-(methoxymethylidene) adamantane, the zwitterionic peroxides of which are readily captured by acetaldehyde [8]. However, the behavior of 1 and 16 parallels that of 2-(phenoxyethylidene) adamantane which always gives 1,2-dioxetane product even in the presence of acetaldehyde [17]. A final difference between 1 and 16 is revealed by their ability to form 1,2,4-trioxanes. The synthesis of both cis- and trans-fused bicyclic trioxanes (e.g. 22 and
25) is possible for 16 through the intermediacy of the 2-hydroperoxy cation 21 derived from 31 and the trans-2-hydroperoxy alcohol 23, resp. Indene (1) only affords the cis-fused trioxanes (12 and 15), through the 2-hydroperoxy cation 6. Inexplicably, trans-fused trioxanes are inaccessible.

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