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FORMATION OF A K-REGION ARENE OXIDE BY INTRAMOLECULAR O ATOM TRANSFER

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Abstract: Intramolecular reaction of the carbonyl oxide 1-benzoylphenanthrene oxide leads to the K-region oxide 1-benzoyl-9,10-epoxy-9,10-dihydrophenanthrene.

We have been studying carbonyl oxides as models for the monooxygenase enzymes (MOX) as originally suggested by Hamilton[1]. It is now reasonably well established that such enzymes are responsible for the metabolic activation of polycyclic aromatic hydrocarbons (PAH)[2-8]. For PAH which are carcinogenic and/or mutagenic such activation leads to the formation of metabolites, i.e. oxidation products of PAH, some of which are now recognized as the ultimate carcinogens with the PAH precursors being considered as pre-carcinogens. We have suggested[9] that polluted atmosphere containing ozone, olefins, and PAH could lead to the activation of PAH in the absence of metabolic processes. Confirmation of this suggestion would add greatly to the anticipated environmental health hazards of such atmospheres.

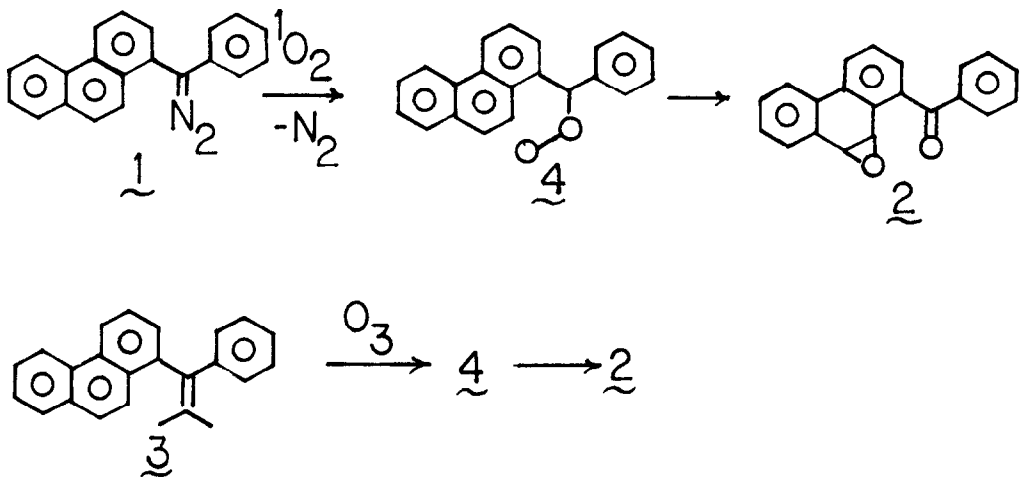
We have shown[10-14] that singlet oxygen oxidation of diazo compounds leads to the formation of carbonyl oxides. Carbonyl oxides produced in this manner are generally more amenable to study as MOX models than are those produced under the conditions of ozonolysis which is the usual route to carbonyl oxides. To date carbonyl oxides have been shown to oxidize aliphatic[15] and aromatic[11,13,14,16,17] hydrocarbons, epoxidize olefins,[12,18] bring about the NIH shift,[16,17] oxidize sulfides[19-22] and sulfoxides,[19-23] and causes oxidative decarboxylation of α-keto carboxylic acids.[24] Thus carbonyl oxides have proven to be viable and useful MOX models.

Intramolecular oxidation by carbonyl oxides has received less attention than intermolecular reactions.[13,14,25] Such reactions are potentially more important to the MOX modelling aspect of these studies because of the proximate nature of the O atom transfer, that is intramolecular oxidation more closely approximates the chemistry of the enzyme-substrate complex. In the present work we describe an intramolecular O atom transfer by a carbonyl oxide to give a K-region oxide. The carbonyl oxide has been produced both by singlet oxygen oxidation of the required diazo compound and by ozonolysis of an appropriate olefin. The latter conditions are of particular importance to our earlier conjecture on atmospheric PAH activation and the subjects of air pollution and environmentally derived carcinogenesis and mutagenesis.

In a typical experiment 1-phenanthrylphenyldiazomethane,[26] 1, was photooxidized[28] in methylene chloride solution using Ⓟ-Rose Bengal as sensitizer. Preparative TLC was used to isolate 1-benzoyl-9,10-epoxy-9,10-dihydrophenanthrene,[29] 2, the K-region oxide, which was identified by comparing TLC R_f, HPLC retention time, NMR, mass spectra, and melting point data

with those of the authentic material.[30] The yield of 2, as determined by HPLC, was 7.12%.[32] Likewise ozonolysis of 1-(1-phenanthryl)-1-phenyl-2-methyl-1-propene,[33] 3, and a similar workup led to the formation of three products one of which was 2 (4.2% yield).

By analogy to the earlier cases[10-14] we conclude that photooxidation of 1 leads to the formation of 1-benzoylphenanthrene oxide, 4. Carbonyl oxide 4 then transfers an O atom intramolecularly to the K-region of the phenanthrene moiety producing the product oxide 2. Ozonolysis of olefin 3 is seen as proceeding in the usual manner. The intermediate 1,2,3-trioxolane (initial ozonide) can decompose *via* two pathways one of which gives carbonyl oxide 4 while the other gives acetone oxide. By analogy to similar cases in the literature[34] we expect the decomposition pathway to give 4 to be slightly favored. The carbonyl oxide, 4, again reacts intramolecularly to give 2.



It is particularly significant we believe that we have shown for the first time that a carbonyl oxide produced *via* ozonolysis, i.e., under conditions more closely approximating those in urban atmospheres, can oxidize an aromatic substrate to produce an arene oxide.

To further examine the possible role of ozone in producing mutagenic or carcinogenic material in polluted atmospheres we have begun a series of experiments involving model particulates. There is now a growing body of evidence[35-41] indicating that PAH absorbed on atmospheric particulate matter can become activated as a result of atmospheric oxidation processes, that is, samples of such materials display a degree of mutagenicity not associated with the unactivated hydrocarbons. While in many cases the precise nature of the oxidant is not clear, Pitts *et al*[42] have been able to show in one such case that ozone can convert benz[a]pyrene which is absorbed on a glass fiber filter to its 4,5-oxide which had previously[43] been shown to be mutagenic. Presumably related to these observations are those[44,45] in which fly ash emitted from coal-fired power plants has been found to contain mutagenic materials.

We have found that when olefin 3 is absorbed on silica gel as a model particulate and then exposed to a O_3/O_2 gas stream the K-region oxide 2 is again produced.[46] In a control experiment we have shown that 1-benzoylphenanthrene similarly absorbed on silica gel and exposed to the O_3/O_2 gas stream is not converted to the oxide. Thus we conclude that 3 is converted to the carbonyl oxide 4, by ozone with subsequent intramolecular O atom transfer to give the arene oxide, 2. These results provide further evidence that carbonyl oxides, produce in polluted atmospheres, may be involved in the non-enzymatic activation of PAH in urban atmospheres.

K-region oxides have been considered to be likely precursors to further *in vivo* reactions leading to carcinogenesis or necrosis because of their increased stability relative to other arene oxides.[47] Presumably increased stability decreases the likelihood of detoxification reactions while favoring those pathways involving covalent bond formation with biopolymers including DNA and RNA. In preliminary work we have found that 2 is considerably more stable than phenanthrene oxide under a variety of conditions. For example no phenols are found among the products when the oxide, 2, is produced by photooxidation of 1, while similar conditions partially convert[9] phenanthrene-9,10-oxide to phenanthrol. We are now investigating the general influence of accompanying oxygen functionality on the stability of arene oxides.

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30. Authentic 2 was prepared via hypochlorite oxidation under phase transfer conditions as described by Hamilton et al.[31] 1-Benzoyl-9,10-epoxy-9,10-dihydrophenanthrene has the following properties: m.p. 192-193°C. ^{1}H NMR ($CDCl_3$): δ 4.40 (d, 1H, J = 4 Hz), 4.53 (d, 1H, J = 4 Hz), 7.2-8.5 (m, 12 H); ^{13}C NMR ($CDCl_3$): 189.6 (s), 142-124 (m), 56.9 (d), 53.1 (d), (ppm); IR ($CHCl_3$); 3060, 1665, 920 cm^{-1}; Mass Spec (% of base); 298 (84), 282 (40), 270 (92), 220 (70), 165 (100), 105 (68), 77 (70), 28 (50).

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