Preparation of Oxepines during Direct Chemical Synthesis and Facile Oxygen Walk Reactions of Arene Oxides: Theoretical Predictions and Experimental Evidence

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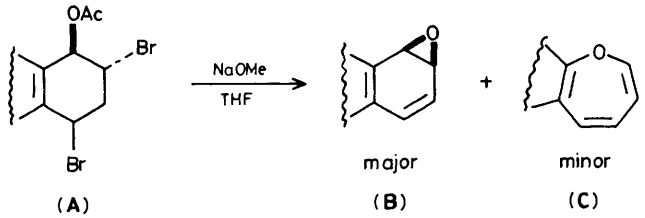
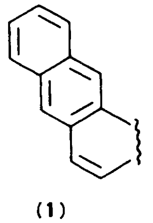
The synthesis of arene oxides and oxepines, and the unexpectedly facile rearrangement of a range of non-K- and bay-region arene oxides of polycyclic aromatic hydrocarbons to isolable isomeric oxepines *via* a photochemical oxygen walk pathway is reported; oxepine formation can be predicted from PMO calculations which indicate the associated loss of resonance energy during the oxygen walk process.

The oxygen walk (or circumambulatory[1]) rearrangement of arene oxides to yield the isomeric oxepines has previously resulted from the u.v. irradiation of the K-region arene oxides of phenanthrene[2,3] and pyrene.[4] To date however a 'spontaneous' oxygen walk processs of a polycyclic aromatic hydrocarbon (PAH) arene oxide has not been observed.[1,5] Both thermal and photochemical rearrangements of arene oxides have frequently resulted in phenol formation.[5]

Arene oxides (**1B**), benz[*a*]anthracene 1,2-oxide,[6] and (**2B**), triphenylene 1,2-oxide,[7] have recently been synthesised during studies of the mechanism and stereochemistry of metabolism of PAHs. The crude product mixtures containing arene oxides (**1B**) and (**2B**) obtained from the dibromoesters (**1A**) and (**2A**) were found also to contain variable quantities of minor impurities (0—20%) which were removed by recrystallization. These minor components have now been separated by preparative t.l.c. (silica gel, $CHCl_3$) and identified as oxepines (**1C**) and (**2C**) by ^1H n.m.r. spectral comparison with an authentic sample of 1-benzoxepine. The previously unreported arene oxides (**B**) and oxepines (**C**) of benz[*a*]anthracene (**3**), dibenz[*a,h*]anthracene (**4**), dibenz [*a,j*]anthracene (**5**) and benzo[*e*]pyrene (**6**) have now been synthesised by similar methods to those used for the compounds (**1B**/**1C**)[6], and (**2B**/**2C**)[7] (Scheme 1).

Two possible routes for the formation of oxepines (**C**) from reaction of the dibromoacetate precursors (**A**) are shown in Scheme 1. Route a involves the 'normal' mechanism for arene oxide formation from a dibromoester precursor followed by

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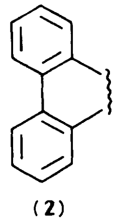
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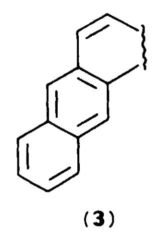
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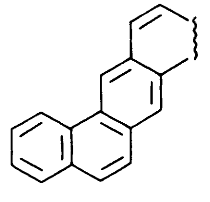
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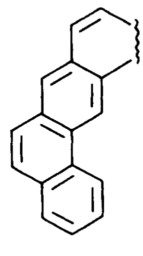
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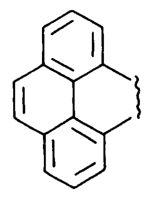
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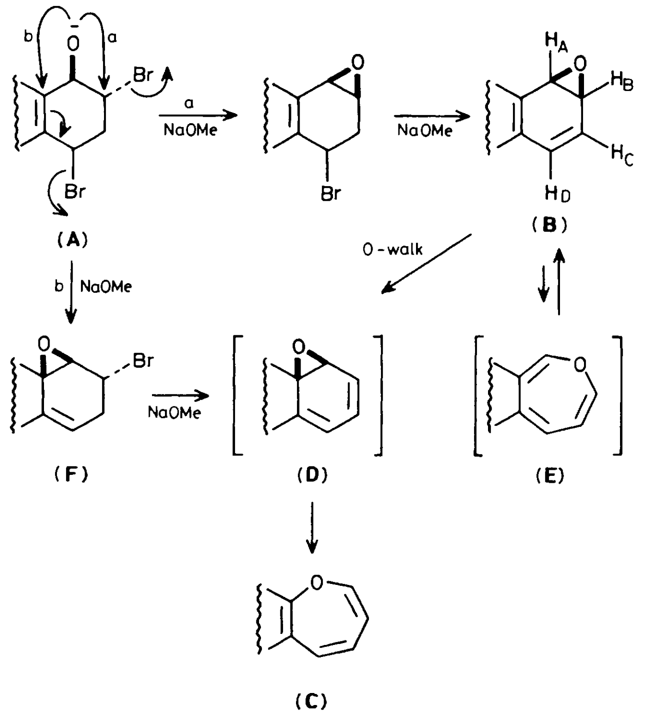

Scheme 1

an oxygen walk rearrangement of arene oxide (**B**) to the unstable arene oxide (**D**) and ultimately oxepine (**C**). An alternative pathway (b) could conceivably involve an S_N2' mechanism[8] to yield a bromo-epoxide (**F**) which is further converted into the unstable arene oxide (**D**) and oxepine (**C**).

^{1}H N.m.r. analysis of the reaction products obtained by treatment of the dibromoacetates (**2A**), (**5A**), and (**6A**) with $NaOCD_3$ was carried out *in situ* using [$^2H_8$]tetrahydrofuran (THF) as solvent in standard n.m.r. sample tubes protected from light. The major products obtained were the arene oxides (**B**) but these were accompanied at all stages of the reaction by a constant proportion of oxepine (**C**) which only varied (between 15 and 40%) among individual experiments.

When these n.m.r. tube samples of arene oxide (**B**) and oxepine (**C**) were allowed to stand in a sunlit portion of the laboratory for several hours, the arene oxide form (**B**) was found to isomerize 'spontaneously' to oxepine (**C**) and the corresponding phenol. Exposure of freshly prepared samples of arene oxides (**B**) (in Pyrex n.m.r. tubes containing standard reference peaks) to u.v. light (Hanovia, Photochemical Reading Reactor, medium pressure lamp, >300 nm, $CDCl_3$, 0.5 h) resulted in a total conversion of arene oxide (**B**) to oxepine (**C**) and the isomeric phenol. This observation provides clear evidence of a photochemically induced oxygen walk process occurring under much milder conditions than reported previously for arene oxides (254 nm).[2—4] Whether the oxygen walk proceeds *via* a stepwise mechanism involving a diradical intermediate or *via* a concerted suprafacial [1,5] sigmatropic rearrangement is presently unknown.†

In view of the consistent formation of oxepine (**C**) from NaOMe treatment of dibromoacetate (**A**) (even in the dark), the additional possibility of an S_N2' mechanism should be considered. The observation that oxepines (*e.g.* **1C**—**6C**) are only obtained during direct synthesis of those arene oxides (*e.g.* **1B**—**6B**) which have very low barriers to racemization,[9] is fully consistent with an S_N2' mechanism. The loss of resonance energy (ΔE_R) associated with the cyclization step (**A**) → (**F**) is similar to that found in the oxygen-walk step (**B**) → (**D**).

The previously reported predictions[9] (for arene oxides **1B**—**6B**), and experimental observations[5—7] that arene oxides (**1B**), (**2B**), and (**3B**) had indeed undergone spontaneous racemization, are related to the loss of resonance energy (ΔE_R) associated with isomerization of the arene oxide (**B**) to the high energy (undetected) oxepine (**E**). The relative loss of resonance energy during the oxygen walk step (**B**) → (**D**) for a range of arene oxides is parallel to the loss of resonance energy found in the reversible electro-cyclization step (**B**) → (**E**). The calculated[9] values for the loss of resonance energy (ΔE_R, kcal mol^{-1}; cal = 4.184 J) in the latter step for arene oxides (**1B**)—(**6B**) are: (**1**) (7.2), (**2**) (4.9), (**3**) (7.2), (**4**) (7.9), (**5**) (7.9), (**6**) (2.7).

The oxepines (**1C**—**6C**) were thus all obtained as co-occurring minor products during the synthesis of arene oxides (**1B**—**6B**) from the dibromoacetate precursors (**1A**)—(**6A**) and from photorearrangement of the arene oxides. These preliminary results indicate that the earlier PMO calculations used to predict relative reacemization barriers for arene oxide enantiomers may now be used to predict the ease of formation of oxepines *via* an oxygen walk pathway or by direct synthesis from dibromoacetates.

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† To be consistent with the Woodward–Hoffmann/Dewar–Zimmerman rules, a concerted photochemical suprafacial [1,5] sigmatropic rearrangement of (**B**) to (**D**) should proceed *via* inversion at the migrating oxygen atom.

It is noteworthy that arene oxides (**1B**—**6B**) have ΔE_R values of <8 kcal mol^{-1} and that more than ten additional examples of arene oxides having similar or lower ΔE_R values (2.3 kcal mol^{-1} for dibenz[*a*,*c*]anthracene 1,2- and 3,4-oxides being the lowest values) are now predicted to undergo this facile oxygen walk process based upon the earlier PMO calculations.[9] Initial photoisomerization experiments on arene oxides with higher ΔE_R values[9] ($\gg$8 kcal mol^{-1}), *e.g.* naphthalene 1,2-oxide and anthracene 1,2-oxide, under identical experimental conditions gave no oxepine products from an oxygen walk pathway.

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