OXIDATION OF SEVERAL AROMATIC HYDROCARBONS USING DIMETHYL SULFOXIDE EXPOSED TO THE ATMOSPHERE*

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Summary:

1,2,5,6-dibenzanthracene and several other carcinogenic aromatic hydrocarbons are oxidized to the corresponding quinone derivatives in basic dimethyl sulfoxide. This oxidation can occur in the absence of molecular oxygen, and also in dimethyl sulfoxide that has not been properly dried.

Introduction:

In the early 1950's, Heidelberger, Hadler, and Wolf[1] conducted biological experiments in which labeled 1,2,5,6-dibenzanthracene (DBA) in benzene solution was applied to the shaved backs of mice. Since the ability of dimethyl sulfoxide (DMSO) to penetrate membranes is well documented[2], and since DMSO has already been used as a carrier solvent for 9,10-dimethyl-1,2-benzanthracene[3], and other polycylic aromatic hydrocarbons[4], we foresaw the necessity of characterizing DMSO as a solvent for carcinogenic hydrocarbons. Preliminary results indicate that under certain conditions, DMSO can oxidize various aromatic hydrocarbons to the corresponding quinone derivatives. We have found that DMSO which has been exposed to the atmosphere for extended periods of time will spontaneously oxidize these aromatic hydrocarbons. When using

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DMSO that has been freshly distilled from calcium hydride, it is necessary to add base to the solution in order to complete the reaction. We have not been concerned here with the actual mechanism by which the reaction proceeds but have noted that oxidation reactions conducted by Russell and co-workers[5] involving DMSO and base require molecular oxygen. The oxidation discussed here does not require molecular oxygen and probably proceeds via a different mechanism. The reaction is easy to observe in most cases, because the quinone product changes the color of the solution from clear to bright yellow. If a small amount of base (aq.) is added to the solution containing DBA in DMSO, the solution immediately changes color. The yellow solution is not formed if the base is added prior to the introduction of the DBA or before the DBA has gone into solution; which may be due to the insolubility of DBA in aqueous solutions, or there is some type of interaction between DMSO and the hydrocarbon that facilitates the attack of the hydroxide ion in the 9,10 position.

Methods and Materials:

All hydrocarbons tested were obtained from Eastman Organic Chemicals, Distillation Products Industries, Rochester, New York, and were not further purified. Reagent grade DMSO was obtained from the J. T. Baker Chemical Company, Phillipsburg, N. J. and was distilled from calcium hydride. Mass spectroscopic determinations were made on a Hitachi Perkin-Elmer RMU-7 Mass Spectrometer Infrared spectra were taken on a Perkin-Elmer 237 Grating Infrared Spectrophotometer using KBr pellet and thin film techniques.

The effect of molecular oxygen was eliminated from the reaction by vacuum distillation (5 microns or better). While the reaction system was maintained under vacuum, DMSO was distilled from CaH_2 into three flasks containing DBA and/or NaOH (solid and

Table 1

Reactions of DBA in Basic DMSO

	DBA	DMSO	Base (NaOH)	Results
1	4mg.	5ml.	none	no reaction (15 min.)
2	4mg.	5ml.	(solid)	DBA crystals nearest pellet turned yellow
3	4mg.	5ml.	10^{-3}ml. 0.1 M	immediate change in color from clear to yellow

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aqueous). The results are tabulated in Table I. The experiments were repeated with molecular oxygen present and the results were identical.

As an example, the product of the reaction of DBA and basic DMSO was determined to be 1,2,5,6-dibenz-9,10-anthraquinone by the following data. After shaking for 48 hours, the spectrum of the yellow solution was recorded and showed strong infrared absorption at 1669 cm^{-1} (C=O). This yellow product was precipitated by dilution with water, washed (H_2O), filtered, and dried. The melting point of the product was determined to be 244-247°. Infrared spectra (KBr) showed strong absorption at 1668 cm^{-1}. The product forms a dark violet solution with conc. H_2SO_4 in agreement with the findings of Roitt and Waters[6]. Mass spectra gives a parent peak of m/e = 308.

Results and Discussion:

The hydrocarbons studied and the results of their reaction with basic DMSO are tabulated in Table 2. It can be seen that no reaction takes place between basic DMSO and 9,10-dimethyl-1,2-benzanthracene. The preferred 9,10 positions are blocked by methyl groups in this case, and the system is not oxidized. Mass spectral data shows that there is a small but detectable

Table 2

Reactions of Aromatic Hydrocarbons in Basic DMSO

Compound	Oxidation	Methylation
1,2,5,6-DBA	+	-
1,2,3,4-DBA	+	-
2,3,6,7-DBA	+	-
1,2-BA	+	+
9,10-dimethylbenzanthracene	-	-
Anthracene	-	-
3,4-benzpyrene	-	-
20-methylcholanthrene	-	-

amount of methylated 1,2-benz-9,10-anthraquinone. 3-methylcholanthrene and 2,3-benzpyrene do not have reactive positions comparable to the 9,10 positions in the dibenzanthracene and benzanthracene systems and show no reaction. We have noted, however, that these two compounds fluoresce in DMSO. The spectra of DBA in basic DMSO shows two overlapping broad bands (Fig. 1) between 5200 and 4400 Å (peaks at 4663 Å and 4950 Å) which are not present in the spectra of either DBA, DMSO, or the isolated quinone. These bands may be due to the presence of a reaction intermediate or a charge transfer species.

DMSO which has been exposed to the atmosphere such as that frequently used to introduce aromatic hydrocarbons to biological systems is easily contaminated and capable of altering certain aromatic hydrocarbons. The nature of the contaminant or change in DMSO which has been exposed to the atmosphere has not been specifically determined. However, DMSO is very hygroscopic[7] and when water is used in place of base, the same color change can be detected, but it is not as intense. The same is true when

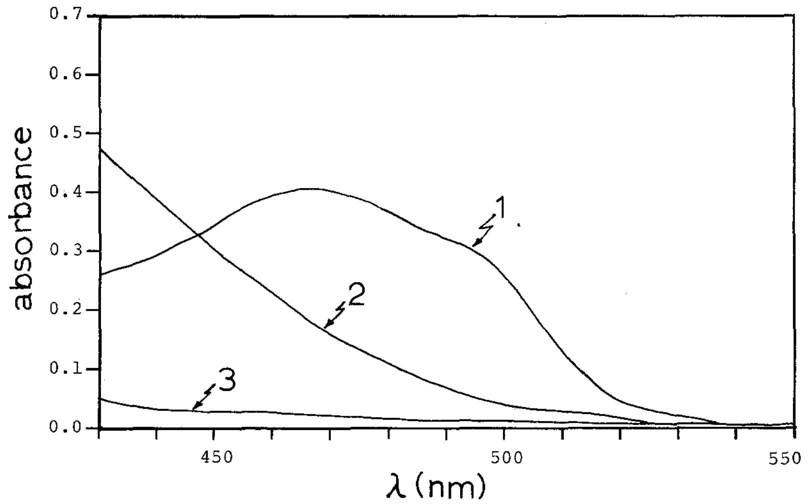

Figure 1. Spectra of (1) DBA in DMSO, (2) 1,2,5,6-dibenz-9,10-anthraquinone in benzene and (3) DBA in benzene.

bases such as calcium hydroxide and sodium bicarbonate are used. No reaction could be detected when pyridine is used.

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