

DIRECT PERACID OXIDATION OF POLYNUCLEAR HYDROCARBONS TO ARENE OXIDES

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(Received in USA 14 July 1976; received in UK for publication 6 January 1977)

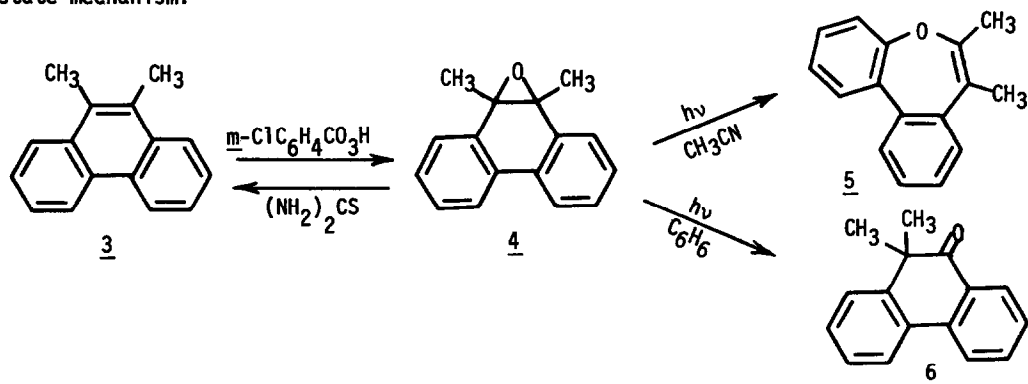
The literature contains reports that peracid oxidation of polycyclic aromatic hydrocarbons leads to formation of K-region arene oxides including those of pyrene and dibenzo[a,h]anthracene.^{1,2} It has been stated, however, that the products isolated were of questionable purity and remained to be characterized definitively.³ On the other hand, a number of procedures have been devised recently for the synthesis of such biographically significant arene oxides from the parent polynuclear hydrocarbons⁴, but all suffer from the disadvantage that they are multi-step in character and in our experience, the immediate precursors may be difficultly accessible, and undesirable complications may interfere. For these reasons we have reinvestigated the possible synthetic utility of direct arene oxidation using *m*-chloroperbenzoic acid as the oxidant.⁵

Previous experience has shown that acenaphthylene may be oxidized to the corresponding oxide under carefully controlled conditions⁶ which suggested that this method could conceivably be extended to less reactive systems. The previous difficulties encountered in isolating the oxide may be attributed primarily to the tendency of the rather acidic by-product, *m*-chlorobenzoic acid, to induce acid catalyzed rearrangement(s) to phenols (or ketones) and/or the tendency for further competitive oxidation to quinone(s), dicarboxylic acid(s), or polyoxides to occur. To avoid such complications, we have utilized a two-phase system composed of aqueous sodium bicarbonate-methylene chloride (or carbon tetrachloride) as the peracid oxidation medium and have achieved the conversions of a spectrum of polynuclear hydrocarbons to arene oxides (see accompanying table) in yields sufficiently high to constitute a practical synthetic laboratory procedure in several cases.

In a typical example, a solution of 1.0 g (5.0 mmol) of *m*-chloroperbenzoic acid⁵ and 0.18 g (1.0 mmol) of phenanthrene (**1**) is stirred vigorously with a mixture of 25 ml of methylene chloride and 25 ml saturated sodium bicarbonate solution at 37-38°C for 2.5 hr. Sodium thiosulfate solution (10 ml; 1 *N*) and 25 ml of methylene chloride were added and stirring was continued for an additional 2 or 3 min. The organic phase was then separated and passed through a column (2 cm) of neutral alumina (activity 3) (10 cm) capped with anhydrous sodium sulfate (10 cm). The column was eluted with 100 ml of methylene chloride and the eluate

concentrated under reduced pressure to approximately 20 ml. A small quantity of alumina (activity 3) was added as an adsorbent and the residual solvent removed *in vacuo* on a rotary evaporator. The alumina, coated with products, is then transferred to a column (activity 3 neutral alumina; 70 g) and chromatographed in the conventional manner using mixtures of ether-hexane (0 ~ 20%) as the eluants. Phenanthrene (19 mg; 11%) elutes first while phenanthrene oxide (2) (114 mg; 59%) emerges later. The latter was identified by comparison with an authentic sample (mass spectrum, NMR, IR, TLC) prepared according to known procedures.^{4a}

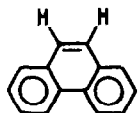
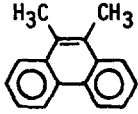
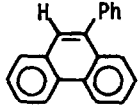
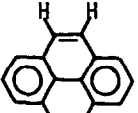
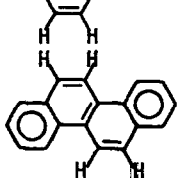
It is significant that the oxidations studied appear to be enhanced by the presence of water although its role remains to be defined. 9,10-Dimethylphenanthrene-9,10-oxide (4) has been previously synthesized, albeit in very low yield (~1%) by treatment of *trans*-9,10-dihydrophenanthrene-9,10-diol with DMF-dimethyl acetal.⁷ The present method clearly has advantages in this particular case. While the NMR, IR, and mass spectral data for the oxide 4 compare favorably with those reported for the arene oxide prepared by direct oxidation of 9,10-dimethylphenanthrene (3)⁸, the melting point observed is somewhat higher (120-121°C; CH_2Cl_2 - C_6H_{14}). On treatment with thiourea in methanol at room temperature, the oxide 4 is cleanly deoxygenated to the parent arene 3,⁹ and undergoes the characteristic "oxygen walk" rearrangement^{3,4b,4h,10,11a,12} upon irradiation in acetonitrile with formation of 6,7-dimethyl-2,3;4,5-dibenzoxepin (5). 10,10-Dimethylphenanthrene-9-one (6) is the major photoproduct when benzene is employed as the solvent. The change in course of the reaction is attributed to solvent sensitization in the latter case and resultant intervention of the triplet excited state mechanism.¹⁰



The structure of 9-phenylphenanthrene 9,10-oxide (8) prepared by oxidation of 9-phenylphenanthrene (7) and purified by TLC (oil) was confirmed by mass spectral (M^+ 270), NMR δ 4.40, 1H, ArCHO-) and IR (no OH or C=O) analyses. Furthermore, deoxygenation to 9-phenylphenanthrene (7) was also achieved as described for 9,10-dimethylphenanthrene 9,10-oxide (4).⁹

As anticipated, with higher homologs of phenanthrene, the oxidation process described herein becomes substantially more complex due to the increased sensitivity of the oxides to further oxidation and decomposition during workup; however, it was possible to isolate

and identify pyrene 4,5-oxide (11)^{4d,4f,11} and chrysene 5,6-oxide (12)^{4f,13} derived from 9 and 10, respectively. The structure of the latter oxide 12 was confirmed by spectral analyses and comparison of NMR data with reported values.^{4f} Furthermore, deoxygenation of 12 to 10 was also achieved in the manner described above.⁹ The bis-arene oxide derived from

TABLE					
Parent arene	$m\text{-ClC}_6\text{H}_4\text{CO}_2\text{H}$ (equiv.)	Temp. (°C)	Time (hr)	Yield (%)	
 <u>1</u>	5	37	2.5	59	
 <u>3</u>	2	25	8	40 ^{a)}	
 <u>7</u>	2	25	10	50	
 <u>9</u>	5	25	3	14	
 <u>10</u>	5	25	0.25	9 ^{b)}	

a) After recrystallization

b) Chromatographed on basic alumina (activity 3)

pyrene is reportedly highly susceptible to rearrangement^{11d} which may account for the difficulties encountered in isolating 11 from the oxidation mixture obtained from 9.

The extension of peracid oxidation to non-K-region oxides also has been achieved. In fact *anti*-naphthalene 1,2:3,4-dioxide¹⁴ may be synthesized in moderate yield.¹⁵ Even alkyl benzenes are oxidized although competing reactions occur and the conditions remain to be developed in order to achieve isolation of the desired products.¹⁵

ACKNOWLEDGMENT. The authors wish to thank the National Institutes of Health (Grant 1-R01-CA18346-01) and the Cancer Association of Greater New Orleans, Inc., for support of this work. They also wish to acknowledge the assistance of Dr. E. Elder and Ms. J. Thompson in the preparation of the manuscript.

REFERENCES AND NOTES

1. E. Boyland and P. Sims, Biochem. J., **90**, 391 (1964).
2. B.L. Van Duuren, I. Bekersky, and M. Lefar, J. Org. Chem., **29**, 686 (1964).
3. D.M. Jerina, H. Yagi, and J.W. Daly, Heterocycles, **1**, 267 (1973).
4. (a) M.S. Newman and S. Blum, J. Am. Chem. Soc., **86**, 5598 (1964); (b) G.W. Griffin, S.K. Satra, N.E. Brightwell, K. Ishikawa, and N.S. Bhacca, Tetrahedron Lett., 1239 (1976); (c) E. Vogel and F.-G. Klärner, Angew. Chem., Int. Ed. Engl., **7**, 374 (1968); Angew. Chem., **80**, 402 (1968); H. Yagi and D.M. Jerina, J. Am. Chem. Soc., **95**, 243 (1973); (d) P. Dansette and D.M. Jerina, ibid., **96**, 1224 (1974); (e) S.H. Goh and R.G. Harvey, ibid., **95**, 242 (1973); (f) R.G. Harvey, S.H. Goh, and C. Cortez, ibid., **97**, 3468 (1975); (g) M.-C. Lasne, S. Masson, and A. Thuillier, Bull. Soc. Chim. Fr., 1751 (1973); (h) private communication from Prof. T. Okamoto; taken in part from the Ph.D. Dissertation of N. Miyata, University of Tokyo (1976).
5. Available from Aldrich Chemical Company, Inc., Milwaukee, Wisconsin, in 85% purity and was used in this form.
6. T.H. Kinstle and P.J. Ihrig, J. Org. Chem., **35**, 257 (1970).
7. D. Avnir, A. Grauer, D. Dinur, and J. Blum, Tetrahedron, **31**, 2457 (1975).
8. P.D. Gardner and H. Sarrafizadeh R., J. Am. Chem. Soc., **82**, 4287 (1960); C.K. Bradsher and W.J. Jackson, Jr., ibid., **76**, 4140 (1954).
9. G.W. Griffin, K. Ishikawa, and S.K. Satra, J. Heterocycl. Chem., **13**, 1976 in press.
10. (a) N.E. Brightwell and G.W. Griffin, J. Chem. Soc., Chem. Commun., 37 (1973); (b) B.J. Dowty, N.E. Brightwell, J.L. Laseter, and G.W. Griffin, Biochem. Biophys. Res. Commun., **57**, 452 (1974); (c) K. Shudo and T. Okamoto, Chem. Pharm. Bull., **21**, 2809 (1973).
11. (a) B.L. Van Duuren, G. Witz, and S.C. Agarwal, J. Org. Chem., **39**, 1032 (1974); (b) H. Cho and R.G. Harvey, Tetrahedron Lett., 1491 (1974); (c) S.C. Agarwal and B.L. Van Duuren, J. Org. Chem., **40**, 2307 (1975); (d) R.M. Moriarty, P. Dansette, and D.M. Jerina, Tetrahedron Lett., 2557 (1975).
12. (a) D.M. Jerina, B. Witkop, C.L. McIntosh, and O.L. Chapman, J. Am. Chem. Soc., **96**, 5578 (1974); (b) P.Y. Bruice, G.J. Kasperek, T.C. Bruice, H. Yagi, and D.M. Jerina, ibid., **95**, 1673 (1973).
13. E. Boyland and P. Sims, Internat. J. Cancer, **2**, 500 (1967).
14. E. Vogel, H.-H. Klug, and M. Schäfer-Ridder, Angew. Chem., Int. Ed. Engl., **15**, 229 (1976); Angew. Chem., **88**, 268 (1976).
15. Details on the direct oxidation of naphthalene and benzene derivatives will be published elsewhere.