rapidly oxidized all diols to quinones. On neutralization, the latter precipitated from solution in relatively pure state. It appears that the DMSO–SO_3 reagent[7] may offer broader applicability than existing methods[13] for the general oxidation of 1,2-diols to 1,2-diones.

Reduction of **3** with lithium aluminum hydride[8] proceeded smoothly and stereoselectively to furnish the expected *trans*-diols; however, **3b** was accompanied by a major proportion (45%) of the cis isomer. This diminished steric preference is likely due to the steric influence of the adjacent 7-methyl group.[14] Fortunately, the *trans*-diols may be separated from the cis isomers through conversion of the latter to acetonides with acetone in the presence of anhydrous copper sulfate.

Conversion to the epoxides was effected under conditions similar to those described in the aliphatic series[9] except that DMA–DMF was employed as reagent only (2.5 equiv) and not as solvent (in order to minimize formation of the unreactive bis adducts), and dimethylformamide or chloroform was used as the solvent.

7,12-Dimethylbenz[*a*]anthracene 5,6-oxide, obtained as almost colorless crystals from benzene–ether–hexane, exhibited the following properties: mp 148° (soften ~139°); nmr[15] (CCl_4) δ 2.78 (s, 3, 7-CH_3), 2.93 (s, 3, 12-CH_3), 4.27 (d, 1, oxirane-H, J = 4 Hz), 4.68 (d, 1, oxirane-H, J = 4 Hz), 7.2–8.1 ppm (m, 8, aromatic); ir (KBr) 11.3 μ (medium–weak); mass spectrum *m/e* 272 (parent peak). *Anal.* Calcd for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 88.07; H, 5.96. This epoxide proved considerably more sensitive than **1a** to both heat and protonic solvents. Thus, **1b** in carbon tetrachloride, though stable at 0°, decomposed completely at room temperature within 1 week. In aqueous acetone, decomposition was virtually complete in 72 hr at ambient temperature. Mild hydrolysis in aqueous acetic acid regenerated **4b** accompanied by its dehydration product, 7,12-dimethylbenz[*a*]anthracen-5-ol.

Benzo[*a*]pyrene 4,5-oxide crystallized from benzene in light straw needles: mp 150° (softens ~135°); nmr ($CDCl_3$) δ 4.70 (d, 1, J = 4 Hz), 4.80 (d, 1, J = Hz), 7.5–8.8 ppm (m, 10, aromatic); ir (KBr) 11.2 μ (medium weak); mass spectrum *m/e* 268 (parent peak). *Anal.* Calcd for $C_{20}H_{12}O$: C, 89.53; H, 4.50. Found: C, 89.32; H, 4.64. A sample of the epoxide in benzene showed only slight decomposition after 1 month at room temperature.

The observed instability of **1b** suggested that the previous failure[16] to synthesize it *via* interaction of 1,4-dimethyl- 2- phenylnaphthalene- 3,2′-dicarboxaldehyde with tris(dimethylamino)phosphine[17] was more due to its facility of decomposition than the inadequacy of the synthetic approach. Reinvestigation confirmed this suspicion, and it was found that with appropriate care the epoxides of interest were also obtainable through this method; the yields are given in Table I. At this time, the two approaches appear complementary, and since **1b** and **1c** represent probably the two most difficult to synthesize types of K-region oxide derived from highly active carcinogens, all such compounds should now be available.

It is tempting to speculate that the comparative instability of **1b** may relate to its carcinogenic activity. Structural features, electronic or steric (*e.g.*, symmetry, ring polarization, ring strain, low steric hindrance), which enhance the chemical reactivity of the oxide ring, may be expected to favor greater facility of interaction with a cellular receptor. On the other hand, excessive reactivity might lead to destruction before initiation of the carcinogenic process. Since the number of K-region oxides known is still quite limited and data on their relative reactivity are lacking, no meaningful decision regarding the relationship among arene oxide structure, chemical reactivity, and carcinogenic activity is yet possible. However, the problem is currently under active investigation.

Acknowledgment. This investigation was supported by Grant No. 71-24 from the Illinois Division of the American Cancer Society. We wish to thank Mr. R. Balick for technical assistance during the initial phase of this research.

(13) S. L. Regen and G. M. Whitesides, *ibid.*, **37**, 1832 (1972).

(14) A mixture of diols of unspecified composition was also reported to be obtained from similar reduction of 7-methylbenz[*a*]anthracene-5,6-quinone: P. Sims, *Biochem. J.*, **105**, 591 (1967).

(15) The lower field singlet is assigned to the 12-CH_3 in recognition of the anticipated steric effect of the aromatic proton in the 1 position.

(16) M. S. Newman and S. Blum, *J. Amer. Chem. Soc.*, **86**, 5598 (1964).

(17) V. Mark, *ibid.*, 1884 (1963).

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Synthesis of Non-K-Region Arene Oxides

Sir:

Since the initial isolation of an arene oxide as an obligatory metabolite of an aromatic hydrocarbon,[1] substantial interest has developed in the biochemistry and pharmacology of arene oxides which have been identified as metabolic intermediates[2] and causative agents in studies on necrosis,[3] mutagenesis,[4] and carcinogenesis.[5] Despite their biological importance only two general synthetic routes to arene oxides have been available.[6] K-Region arene oxides have been prepared by closure of the corresponding dialdehydes with tris(dimethylamino)phosphine.[7] In spite of its wide use,[8]

(1) D. M. Jerina, J. W. Daly, B. Witkop, P. Zaltzman-Nirenberg, and S. Udenfriend, *J. Amer. Chem. Soc.*, **90**, 6525 (1968); *Biochemistry*, **9**, 147 (1970).

(2) J. K. Selkirk, E. Huberman, and C. Heidelberger, *Biochem. Biophys. Res. Commun.*, **43**, 1010 (1971); P. L. Grover, A. Hewer, and P. Sims, *Fed. Eur. Biochem. Soc. Lett.*, **18**, 76 (1971).

(3) B. B. Brodie, W. D. Reid, A. K. Cho, G. Sipes, G. Krishna, and J. R. Gillette, *Proc. Nat. Acad. Sci. U. S.*, **68**, 160 (1971).

(4) B. N. Ames, P. Sims, and P. L. Grover, *Science*, 176, 47 (1972).

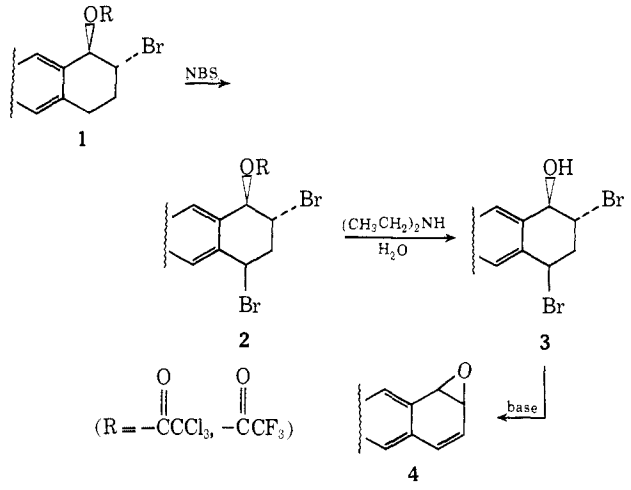
(5) H. Marquardt, T. Kuroki, E. Huberman, J. Selkirk, C. Heidelberger, P. Grover, and P. Sims, *Cancer Res.*, **32**, 716 (1972); P. L. Grover, P. Sims, H. Huberman, H. Marquardt, T. Kuroki, and C. Heidelberger, *Proc. Nat. Acad. Sci. U. S.*, **68**, 1098 (1971).

(6) The accompanying article by Goh and Harvey also represents a new synthesis of arene oxides. We thank these authors for delaying their paper in order that the present results might appear simultaneously. Other syntheses have been reported but are neither preparative nor general. Thus, naphthalene oxide has been prepared by direct oxidation of naphthalene (D. M. Jerina, D. R. Boyd, and J. W. Daly, *Tetrahedron Lett.*, 457 (1970)) and several hindered oxepins have been prepared by the dehydration of 1,4-dihydroxycyclohexadienes (S. Berger, G. Henes, and A. Rieker, *ibid.*, 1257 (1971)).

(7) M. S. Newman and S. Blum, *J. Amer. Chem. Soc.*, **86**, 5559 (1964).

the procedure is limited to K-region oxides.[9] Dehydrohalogenation routes have been utilized for the preparation of non-K-region arene oxides.[10,11] The major difficulty is the instability of a typical intermediate, such as tetralin 1,2-epoxide, under the conditions of bromination with *N*-bromosuccinimide.[12] We have now solved this problem by using halohydrin esters which are stable to the bromination conditions.

The ester blocking groups of choice were trichloro- and trifluoroacetates which allowed their facile removal in the presence of the highly reactive benzylic bromine. Subsequent base treatment introduced both the unsaturation and the epoxide ring in a single step.



Naphthalene 1,2-oxide was prepared with great ease and in excellent yield by this procedure, starting with 1-hydroxy-2-bromotetralin which was acetylated with trifluoroacetic anhydride in $CHCl_3$ to yield **1** (bp 100–105° (0.2 mm), 84%),[13] convertible with surprising ease[14] and in excellent yield (with *N*-bromosuccinimide) to the dibromide **2** (mp 89–90° from petroleum ether, 87%) which was hydrolyzed with aqueous diethylamine in acetonitrile to **3** (mp 109–110° from petroleum ether, 90%). On treatment with dry $NaOCH_3$ in tetrahydrofuran, both the epoxide ring and the double bond were generated in one step to yield naphthalene 1,2-oxide (yield 97%).[15] The overall yield in this procedure is 65% for four steps compared with 14% for three steps by the earlier route from the same starting material.[12,14]

(8) See the examples in ref 7 as well as E. Boyland and P. Sims, *Biochem. J.*, **97**, 7 (1965).

(9) Attempts in this laboratory to cyclize α-chloromuconic dialdehyde to 3-chlorobenzene oxide and *o*-formylcinnamaldehyde to naphthalene oxide with the phosphine reagent have been without success.

(10) E. Vogel and H. Gunther, *Angew. Chem., Int. Ed. Engl.*, 6, 385 (1967).

(11) For further examples, see R. M. DeMarinis and G. A. Berchtold, *Chem. Commun.*, 810 (1971); N. Kaubisch, J. W. Daly, and D. M. Jerina, *Biochemistry*, 11, 3080 (1972); R. Schubart, Ph.D. Thesis, Universität zu Köln, 1967.

(12) E. Vogel and F. G. Klärner, *Angew. Chem., Int. Ed. Engl.*, 7, 374 (1968).

(13) Unless otherwise stated, all new compounds were obtained analytically pure and had satisfactory nmr (Varian 60 MHz) and mass spectra (Hitachi RMU-7, 70 eV). Yields are based on material which showed no detectable impurities by nmr.

(14) The reported yield[12] for the bromination of tetralin 1,2-epoxide with *N*-bromosuccinimide is 23%. While somewhat higher yields (*ca.* 30%) have been observed in this laboratory, very often the reaction fails to initiate and an undefined polymer along with 2-tetralone, *via* rearrangement of the starting oxide, result. Cyclization of **1** (R = H) to tetralin 1,2-epoxide with sodium ethoxide proceeds in ~75% yield of distilled product.

(15) No impurities could be detected by nmr, and the material was identical in all respects with an authentic sample.

The value of the new method was further proven by the successful preparation of the dibromo ester precursors to the unknown 1,2- and 3,4-oxides of phenanthrene from the corresponding halohydrin trichloroacetates of **1**; yields for the *N*-bromosuccinimide reaction to produce the analogs of **2** were 53 and 82%, respectively. For the sequence leading to phenanthrene 3,4-oxide, the dibromo ester **2** was hydrolyzed with aqueous diethylamine in acetonitrile to the alcohol **3** which, without purification, was converted to the desired oxide[16] by diazabicyclononene[12] in overall yield of 70% for the two steps. Attempts to prepare the 3,4-oxide by the conventional route, *viz.*, bromination of 3,4-epoxy-1,2,3,4-tetrahydrophenanthrene, have been completely without success owing to the instability of the tetrahydroepoxide.

However, phenanthrene 1,2-oxide could not be prepared by the new procedure because the bromine in the 4 position of the trichloroacetate ester **2** is too reactive and undergoes side reactions prior to hydrolysis at C-1.[17] Fortunately, 1,2-epoxy-1,2,3,4-tetrahydrophenanthrene is readily brominated at the hindered, benzylic 4 position. Dehydrohalogenation[12] of the crude material gave the desired 1,2-oxide[18] in 61% overall yield for the two steps. The old and the new routes to these two new arene oxides of phenanthrene complement each other to advantage.

A report has appeared describing routes to the 7,8- and 9,10-oxides of the carcinogen benzo[*a*]pyrene[19] by an adaption of the original synthesis of naphthalene oxide.[12] The products obtained were highly impure and could only be characterized tentatively. The synthesis of these oxides by the present procedure is in progress.

(16) The synthesized phenanthrene 3,4-oxide (crystallized from ether–petroleum ether) gave an elemental analysis within 0.2% of theory and an nmr spectrum (CS_2 solvent) which was assigned as 1 H_3, 4.07, 1 H_4 5.02, 1 H_2 6.44, 1 H_1 6.80, and six aromatic protons 7.10–8.30; $^3J_{1,2}$ = 9.0, $^3J_{2,3}$ = 3.5, $^3J_{3,4}$ = 3.5, and $^4J_{2,4}$ = 1.5 Hz. The high instability of this material at room temperature precluded measurement of its mass spectrum or melting point.

(17) The more labile trifluoroacetate also proved unsatisfactory.

(18) The synthesized phenanthrene 1,2-oxide (mp 110–111° from ether) gave an elemental analysis within 0.2% of theory, a mass spectrum with the molecular ion (*m/e* 194) as the base peak and fragments resulting from loss of 18 and 29, and an nmr spectrum ($CDCl_3$ solvent) which was assigned as 1 H_2 4.25, 1 H_1 4.67, 1 H_3 6.63, and 1 H_4 and six aromatic protons 7.30–8.40; $^3J_{1,2}$ = 4.0, $^3J_{2,3}$ = 4.0, $^3J_{3,4}$ = 10, and $^4J_{2,4}$ = 1.5 Hz.

(19) J. F. Waterfall and P. Sims, *Biochem. J.*, **128**, 265 (1972).

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Photochemistry of α-Pyrone in Argon at 8°K[1]

Sir:

Physical evidence for the electrocyclic opening of the α-pyrone ring system is marginal.[2] With this in mind we have reexamined this system.

Irradiation (Pyrex filter) of α-pyrone matrix isolated in argon (1:400) at 8°K leads rapidly to formation of the aldehyde–ketene (Figure 1). Under these conditions

(1) Photochemical Transformations. XLVII. See also R. G. S. Pong and J. S. Shirk, *J. Amer. Chem. Soc.*, **95**, 248 (1973).

(2) O. L. Chapman and C. L. McIntosh, *ibid.*, **95**, 247 (1973).