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OXIDATION OF 4,5-DIHYDROBENZO[a]PYRENE WITH OSMIUM TETROXIDE. STEREOCHEMISTRY OF A SUBSTITUTED K-REGION DIOL.

J. V. Silverton, P. M. Dansette, and D. M. Jerina*
National Heart and Lung Institute
National Institute of Arthritis, Metabolism, and Digestive Diseases
National Institutes of Health
Bethesda, Maryland 20014

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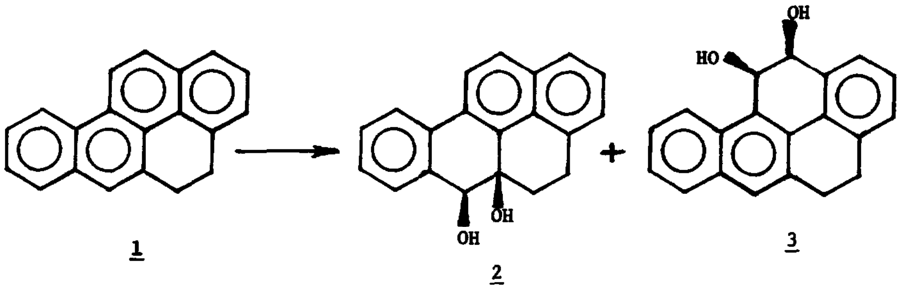
Two recent reports by Jacquignon et al.[1] have described the reaction of osmium tetroxide with dibenzo[a,e]fluoranthene at the 5,5a-K-region[2] to produce an osmate ester which was claimed to yield a trans diol on alkaline hydrolysis based on ir and nmr spectral data. The authors go further to suggest that all reactions of osmium tetroxide at the K-region of aromatic hydrocarbons produce trans diols despite the large body of literature which indicates these diols are cis[3]. An unusual feature of dibenzo[a,e]fluoranthene case is that the K-region which reacts with osmium tetroxide bears a substituent. In the course of our own studies on the synthesis of potential metabolites from the environmental carcinogen benzo[a]pyrene, we have had reason to react 4,5-dihydrobenzo[a]pyrene (1) with osmium tetroxide.[4] Diols were formed at each K-region (2 and 3). The stereochemistry of diol 2 at the substituted K-region was proved to be cis by X-ray crystallography.



Reaction of 1[5] with a molar equivalent of osmium tetroxide in pyridine at rt for 8 days followed by reductive cleavage of the osmate ester[6] provided a mixture (ca. 1:1) of diols 2 and 3. Diol 2 can be isolated from the mixture by fractional crystallization from tetrahydrofuran: 220 MHz nmr (acetone-d_6), $2H_4$ 3.1(m), $2H_5$ 2.3 (m), 5H aromatic 7.49, 2H aromatic 7.9, 2H aromatic 8.09 (m), H_6 4.80 (d $J_{H,OH}$=9.1), OH_6 4.36 (d $J_{H,OH}$=9.4), OH_{5a} 3.76 (s); m/e (chemical ionization, N_2-NO), 288 (100), 270 (16), 257 (7); mp 205-208°; Anal. C,H: $C_{20}H_{16}O_2$. The Infrared spectra of diol 2 in KBr showed broad OH bands at 3320 and 3240 cm^{-1}; in CS_2 solution (1mM), these bands disappeared and were replaced by sharp peaks at 3540 and 3570 cm^{-1} while at 0.1 mM an additional small peak at 3660 cm^{-1} appeared.

The diols 2 and 3 are more easily separated by chromatography (silica gel, chloroform) after acetylation (acetic anhydride-pyridine, rt) since 2 is only monoacetylated at the secondary hydroxyl group. The monoacetate of 2 gave: 100 MHz nmr ($CDCl_3$) CH_3CO 2.40 (s), $2H_4$ 3.2 (m), $2H_5$ 2.0 (m), H_6 6.21 (s); 5H aromatic 7.75 (m), 2H aromatic 7.9 (m), 2H aromatic 8.04 (m); UV λ_{max}^{MeOH} (log ε), 260 (4.67) 270 (4.82), 300 (4.01), 311 (4.08), 324 (3.96); m/e (chemical ionization, N_2-NO) 330 (100), 312 (5), 288 (5), 270 (5); mp 141-142°; Anal. C,H: $C_{22}H_{18}O_3$.

Diol 2 fails to react with periodate under conditions where diol 3 and other K-region diols are readily cleaved.[7] Furthermore, 2 was not converted into a dioxolane with either 2,2-dimethoxypropane[8] or trimethylorthoacetate.[9] These negative reactions cannot be taken as evidence for trans stereochemistry, nor does the above spectral data allow an assignment of relative stereochemistry.

Crystals of 2 were grown in ethyl acetate for X-ray analysis. The space group was $P2_1/c$ with the following cell dimensions: a=12.068 (1), b=5.1363 (4), c=23.982 (2) A°, β=99.324 (7)°. Although the crystals were in the form of fine needles, elongated along b, and the largest crystal obtainable had a cross section of 0.04 x 0.08 mm^2, adequate X-ray data were obtained with an automatic diffractometer (1073 reflections were observed at the 2σ level). The structure was solved readily by previously reported direct methods.[10] A final R-factor of 5.2% was obtained. All hydrogen atoms were found from a difference map and were included in the calculation, although not refined. An ORTEP (11) drawing of the structure is given in Figure 1, and the configuration of the hydroxyl groups was established to be cis ($O_1C_{5a}-C_6O_2$ torsion angle = -63°). The molecules form doubly hydrogen bonded dimers across a center of symmetry, and are linked by a further hydrogen bond along the b axis as shown in Figure 2. The acicular crystal habit is probably accounted for by the hydrogen bonding.

In conclusion, the long held view that osmium tetroxide reacts by cis addition with olefins and K-regions of aromatic hydrocarbons to form osmate esters should not be considered challenged, even if the K-region bears a substituent. If the studies in the fluoranthene series[1] which suggest formation of trans diols are correct, a possible mechanism for their formation would consist of inversion of configuration of an initial cis osmate ester by attack of hydroxide at carbon. Such an inversion pathway may be prevalent at the K-region of the highly strained fluoranthene hydrocarbons.

Angles at carbon atoms in degrees. E.s.d.s are less than 0.5 degrees.

2	1	12a	120.5	1	2	3	121.6	2	3	3a	119.6	3	3a	3b	120.9
3b	3a	4	119.7	4	3a	5a	119.4	3a	3b	12a	118.5	3a	3b	5b	122.8
5b	3b	12a	118.6	3a	4	5	111.1	4	5	5a	110.6	5	5a	5b	111.6
5	5a	01	108.6	5b	5a	01	105.9	5b	5a	6	108.0	8	5a	01	110.4
8	5a	5	112.1	3b	5b	10b	121.8	3b	5b	5a	118.2	5a	5b	10b	120.0
5a	6	02	110.5	5a	6	6a	111.5	6a	6	02	109.6	6	6a	7	123.4
6	6a	10a	116.2	7	6a	10a	120.4	6a	7	8	119.6	7	8	9	120.6
8	9	10	119.6	9	10	10a	121.2	10	10a	6a	118.7	10	10a	10b	122.2
6a	10a	10b	119.0	5b	10b	11	118.0	5b	10b	10a	120.0	10a	10b	11	121.9
10b	11	12	121.7	11	12	12a	121.7								

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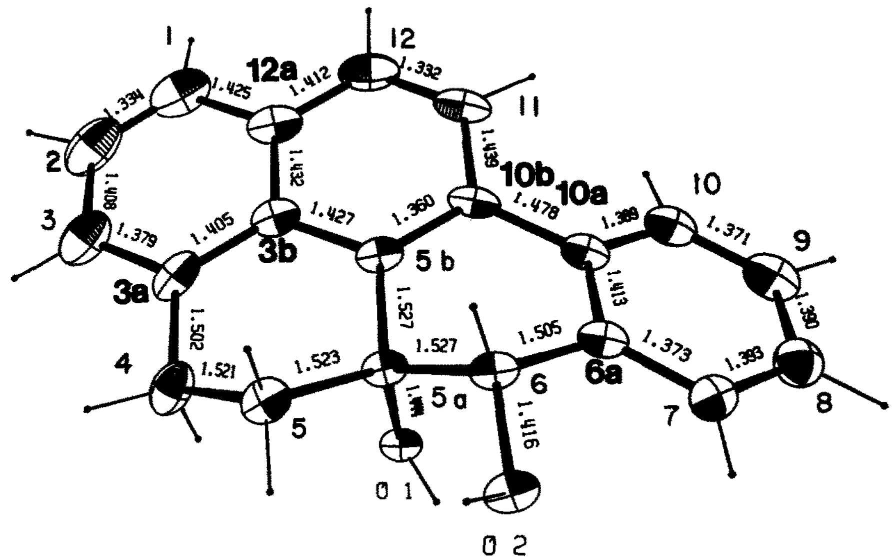

Figure 1. Molecular structure. All bond lengths have e.s.d.s less than 0.01A.

Figure 2. Molecular packing in the crystal. The projection is down b.

Atomic parameters for the heavier atoms(x10⁴). The temperature factor used had the form:

$$\exp -2\pi^2[\Sigma_i \Sigma_j h_i h_j a_i^* a_j^* U_{ij}]$$

Atom	x/a	y/b	z/c	U11	U22	U33	U12	U13	U23
C(1)	4770(5)	-1068(11)	3307(2)	106(5)	65(4)	129(5)	-20(4)	-50(4)	3(4)
C(2)	4251(4)	-550(12)	3745(3)	78(4)	80(5)	178(6)	-18(4)	-25(4)	4(5)
C(3)	4762(4)	969(9)	4205(2)	70(3)	66(4)	137(4)	-4(3)	-7(3)	3(3)
C(3a)	5833(3)	1916(8)	4210(2)	49(3)	36(3)	112(3)	3(3)	-11(3)	1(3)
C(3b)	6416(3)	1410(7)	3760(2)	69(3)	24(3)	68(3)	9(2)	-19(2)	5(2)
C(4)	6399(3)	3418(8)	4715(2)	55(2)	58(3)	111(3)	4(3)	20(2)	-20(3)
C(5)	7268(3)	5293(7)	4552(1)	65(2)	37(3)	75(2)	14(2)	2(2)	-12(2)
C(5a)	8118(3)	3847(6)	4262(1)	57(2)	18(2)	51(2)	10(2)	-8(2)	-1(2)
C(5b)	7542(3)	2258(6)	3759(1)	64(3)	16(2)	52(2)	3(2)	-15(2)	1(2)
C(6)	8949(3)	5697(7)	4050(1)	62(2)	19(2)	49(2)	3(2)	-8(2)	-3(2)
C(6a)	9773(3)	4246(7)	3757(1)	78(3)	21(3)	44(2)	9(2)	3(2)	11(2)
C(7)	903(4)	4778(8)	3838(1)	67(3)	51(3)	65(3)	-2(3)	11(2)	13(2)
C(8)	1606(3)	3323(11)	3552(2)	83(3)	75(4)	77(3)	1(3)	31(3)	21(3)
C(9)	1175(4)	1328(9)	3189(2)	128(4)	57(4)	71(3)	14(4)	43(3)	10(3)
C(10)	46(4)	807(8)	3109(1)	108(3)	44(3)	53(2)	-6(3)	22(3)	7(2)
C(10a)	9324(3)	2231(8)	3387(1)	82(3)	31(3)	44(2)	11(3)	11(2)	10(2)
C(10b)	8116(3)	1596(7)	3337(1)	95(3)	21(3)	36(2)	11(2)	-9(2)	2(2)
C(11)	7534(4)	129(8)	2868(1)	124(4)	48(3)	45(2)	4(3)	-12(3)	-2(2)
C(12)	6482(5)	-688(9)	2854(2)	127(4)	51(3)	68(3)	-19(3)	-44(3)	-7(3)
C(12a)	5878(4)	-133(8)	3297(2)	95(4)	41(3)	77(3)	-6(3)	-35(3)	3(3)
O(1)	8705(2)	1988(4)	4654(1)	57(1)	22(2)	43(1)	6(1)	-4(1)	0(1)
O(2)	9539(2)	7161(4)	4505(1)	64(1)	18(2)	62(1)	8(1)	-18(1)	-8(1)