Bay Region Diol Epoxides of Benzo[*c*]phenanthrene: Force-field Molecular Structures

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The molecular structures of the diequatorial and diaxial conformers of the *syn*- and *anti*-benzo[*c*]phenanthrene 'fjord-region' diol epoxide diastereoisomers have been determined by the Allinger force-field program. Certain features of steric crowding in the 'fjord-region' of the molecule that contribute to relative conformer stability are discussed.

THE structures of polycyclic aromatic hydrocarbons (PAH) are of interest in investigations aimed at elucidating carcinogenic structure–activity relationships.[1] The topological arrangement of the six-membered rings of PAH has important implications with respect to the relative carcinogenicity of different molecules. The relationships between molecular topology and relative carcinogenicity has been the subject of both K-region [2] and bay-region [3] theories of carcinogenicity.

Recent investigations [4,5] have focused on the tumorigenicity and mutagenicity of the dihydrodiols and diol-epoxides of benzo[*c*]phenanthrene (BCP) (Figure 1).

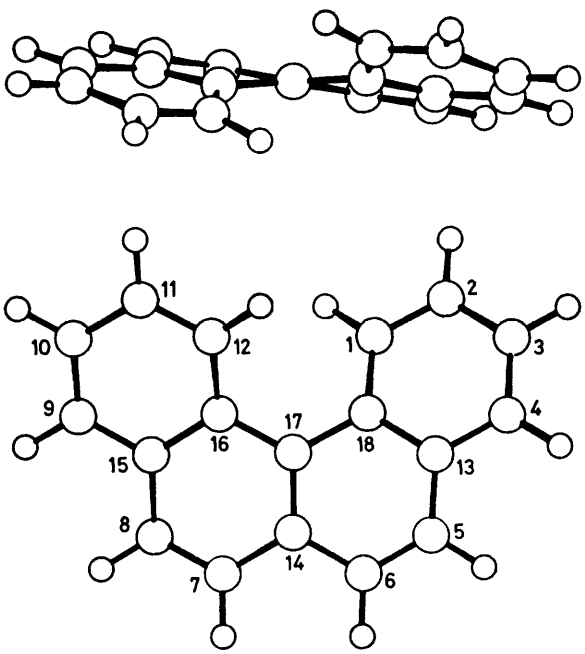

FIGURE 1 Benzo[*c*]phenanthrene (BCP)

Dihydrodiols and diol epoxides have been implicated as proximate and ultimate carcinogenic metabolites of PAH.[6] BCP is a molecule of special interest since the severe steric crowding in the fjord-region that is responsible for deviations from molecular planarity appears to be responsible for the comparable carcinogenic and mutagenic activity [4,5] of the *syn*- and *anti*-diastereoisomers of the fjord-region diol epoxide. Steric crowding in the fjord-region apparently forces the hydroxy-groups of the *syn*-diastereoisomer to adopt a quasi-diequatorial conformation (Figure 2).

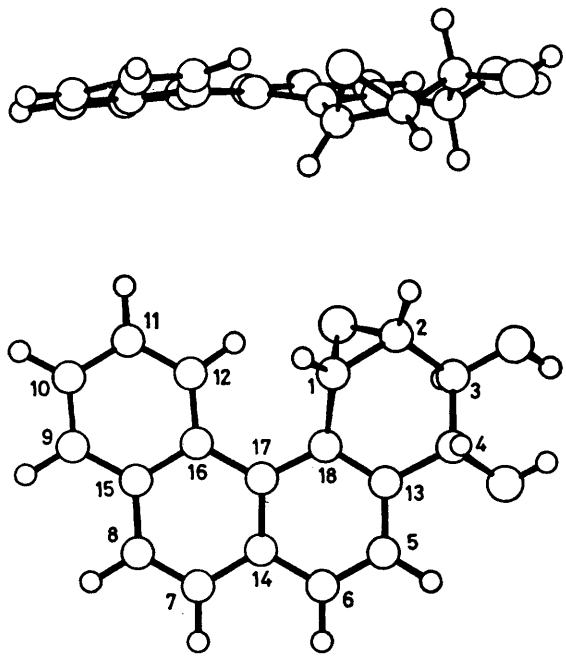

FIGURE 2 *syn*-Diequatorial BCP diol epoxide conformer (3,4-diol 1,2-epoxide)

This paper reports the results of a force-field determination of the structures of the fjord-region diol epoxides of BCP. Certain features involving steric crowding in the fjord-region of the molecule that contribute to relative conformer stability will be discussed. A comparison between the force-field-determined structure of the parent molecule and *X*-ray structural results will also be given.

METHOD

The structures of the fjord-region epoxide conformers of BCP have been determined with the use of the Allinger force-field program.[7] The Allinger force-field parameters have been extended by the addition of an oxiran parameter set provided by Jorgensen and Snyder.[8] Diol epoxide structures were obtained by adding the hydroxy-groups to the force-field-determined epoxide structures. The orientations of the hydrogen of the hydroxy-groups were determined by the CNDO/2 molecular orbital program.[9] The force-field

program has been shown [10] to yield good agreement between the calculated structure of the *anti*-diequatorial bay-region diol epoxide of benzo[*a*]pyrene (BP) and the *X*-ray-determined structure.[11]

RESULTS AND DISCUSSION

Table 1 lists the force-field-determined bond lengths of BCP along with the *X*-ray scattering results from a monomolecular [12] and charge-transfer [13] crystal. One notes that the bond-length differences observed by *X*-ray scattering are paralleled closely by the force-field results. Table 2 lists three non-bonded distances across the fjord-region. The force-field-determined distances are com-

TABLE 1

Bond lengths (Å) of benzo[*c*]phenanthrene

Bond	Force-field	Ref. 12	Ref. 13
C(1)–C(2)	1.38	1.38	1.37
C(1)–C(18)	1.42	1.43	1.41
C(2)–C(3)	1.41	1.41	1.39
C(3)–C(4)	1.38	1.37	1.36
C(4)–C(13)	1.42	1.39	1.41
C(5)–C(13)	1.44	1.44	1.43
C(5)–C(6)	1.37	1.34	1.34
C(6)–C(14)	1.44	1.43	1.43
C(13)–C(18)	1.41	1.43	1.42
C(14)–C(17)	1.40	1.41	1.42
C(16)–C(17)	1.45	1.45	1.45

TABLE 2

Non-bonded distances (Å) across the fjord-region: benzo[*c*]phenanthrene

	Force-field	Ref. 12
C(1)–C(12)	3.04	3.03
C(1)–H(12)	2.59	2.53
H(1)–H(12)	2.33	2.04

TABLE 3

Cartesian co-ordinates (Å): *syn*-diequatorial fjord-region diol epoxide (Figure 2)

Atom	*x*	*y*	*z*
C(1)	0.9359	1.4596	0.5959
C(2)	2.2417	2.0793	0.3501
C(3)	3.2752	1.1740	−0.2934
C(4)	3.1435	−0.2225	0.3130
C(5)	1.5851	−2.1775	−0.0873
C(6)	0.3168	−2.7223	−0.1342
C(7)	−2.1340	−2.4875	−0.0003
C(8)	−3.2482	−1.7157	0.1245
C(9)	−4.3255	0.5075	0.1206
C(10)	−4.2646	1.8810	−0.0392
C(11)	−3.0254	2.4884	−0.3224
C(12)	−1.8674	1.7262	−0.3581
C(13)	1.7542	−0.7888	0.1091
C(14)	−0.8223	−1.8836	−0.0576
C(15)	−3.1457	−0.2768	0.0671
C(16)	−1.8820	0.3397	−0.0640
C(17)	−0.6725	−0.4811	−0.0138
C(18)	0.6395	0.0436	0.1752
O(12)	1.1132	2.4084	−0.4596
O(3)	4.5496	1.7000	−0.1722
O(4)	4.0978	−1.0501	−0.2526
H(1)	0.3618	1.8174	1.4603
H(2)	2.5818	2.9161	0.9765
H(3)	3.0636	1.1633	−1.3713
H(4)	3.3087	−0.1876	1.3983
H(5)	2.4552	−2.8376	−0.1334
H(6)	0.2062	−3.8068	−0.2191
H(7)	−2.2373	−3.5763	−0.0023
H(8)	−4.2283	−2.1940	0.2073
H(9)	−5.2997	0.0362	0.2754
H(10)	−5.1760	2.4858	−0.0042
H(11)	−2.9929	3.5631	−0.5291
H(12)	−0.9632	2.2411	−0.6723
HO(3)	5.1946	1.1643	−0.6016
HO(4)	4.9501	−0.6942	−0.0673

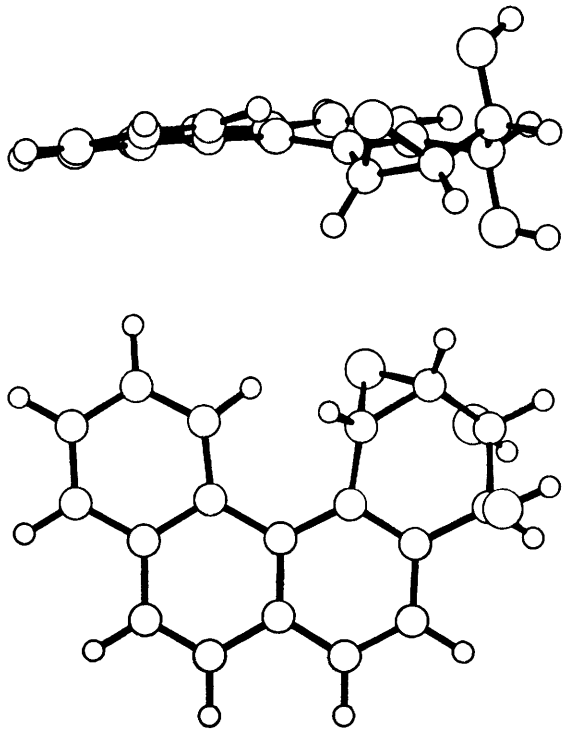

FIGURE 3 *anti*-Diaxial BCP diol epoxide conformer (3,4-diol 1,2-epoxide)

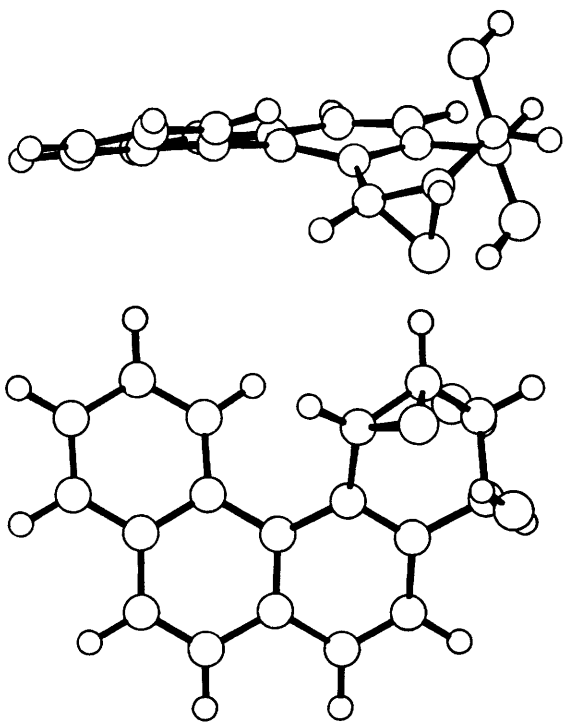

FIGURE 4 *syn*-Diaxial BCP diol epoxide conformer (3,4-diol 1,2-epoxide)

TABLE 4

Non-bonded distances (Å) across the fjord-region of diol epoxides of benzo[*c*]phenanthrene

	H(1)–H(12)	H(1)–C(12)	H(12)–C(1)	C(1)–C(12)	H(12)–O(12)
syn-diequatorial; *anti*-diaxial	2.55	2.88	2.41	2.97	2.09
syn-diaxial; *anti*-diequatorial	2.35	2.61	2.56	3.04	3.93

pared with the *X*-ray determined distances of the monomolecular crystal. One notes the close agreement of the distances between carbon atoms.

Table 3 lists the force-field-determined Cartesian co-ordinates * for the *syn*-diequatorial fjord-region diol epoxide (Figure 2). This conformer of the *syn*-diastereoisomer is stabilized due to steric crowding in the fjord-region. Table 4 lists certain non-bonded distances across

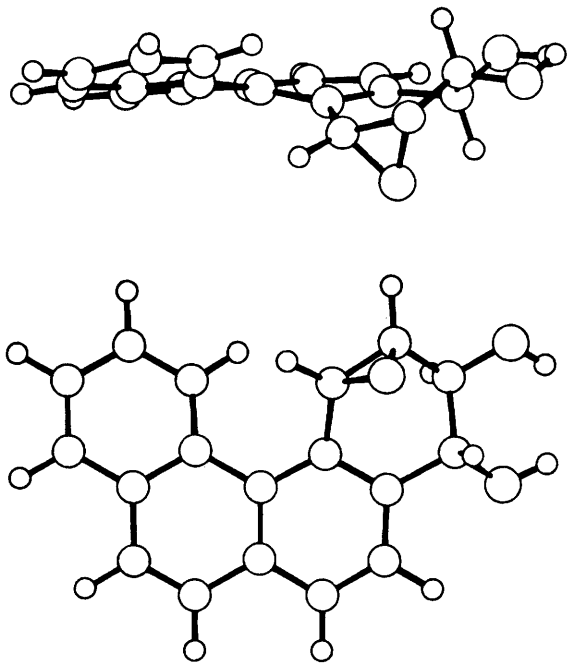

FIGURE 5 *anti*-Diequatorial BCP diol epoxide conformer (3,4-diol 1,2-epoxide)

the fjord-region for the diol epoxides of BCP (Figures 2—5). A comparison of the H(1)—H(12) distances indicates greater steric crowding between the two hydrogen atoms in the fjord-region of the *syn*-diaxial and *anti*-diequatorial conformers compared with the *syn*-diequatorial and *anti*-diaxial conformers. This is responsible for the stabilization of the *syn*-diequatorial conformer with respect to the *syn*-diaxial conformer. The strain energy of the *syn*-diequatorial conformer is found to be *ca.* 5 kcal mol^{-1}† lower than the strain energy of the *syn*-diaxial conformer. One finds a similar stabilization of the *anti*-diaxial conformer with respect to the *anti*-diequatorial conformer. The *anti*-diaxial fjord-region diol epoxide of BCP has apparently not been observed.[4,5]

Conclusions.—The molecular structures of the fjord-region diol epoxides of BCP have been determined with the use of the Allinger force-field program.[7] Steric crowding in the fjord-region of the diol epoxides is shown to significantly distort the molecules from planarity. Steric crowding in the fjord-region of the *syn*-diastereoisomer is found to stabilize the diequatorial with respect to the diaxial conformer. A complete set of Cartesian co-ordinates is given for the sterically crowded *syn*-diequatorial fjord-region diol epoxide of BCP.

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* Cartesian co-ordinates of the other diol epoxide conformers are available by request.

† 1 cal = 4.184 J.

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