

STUDY OF ENERGIES AND GEOMETRIES OF DIBENZO[*a,h*]PYRENE, ITS EPOXIDES AND RELATED COMPOUNDSMaria-Jesús J. RIOSERAS-GARCIA¹ and Jose-Maria HERNANDO-HUELMO^{2,*}*Departamento de Química Física, Universidad de Valladolid, 47005 Valladolid, Spain;
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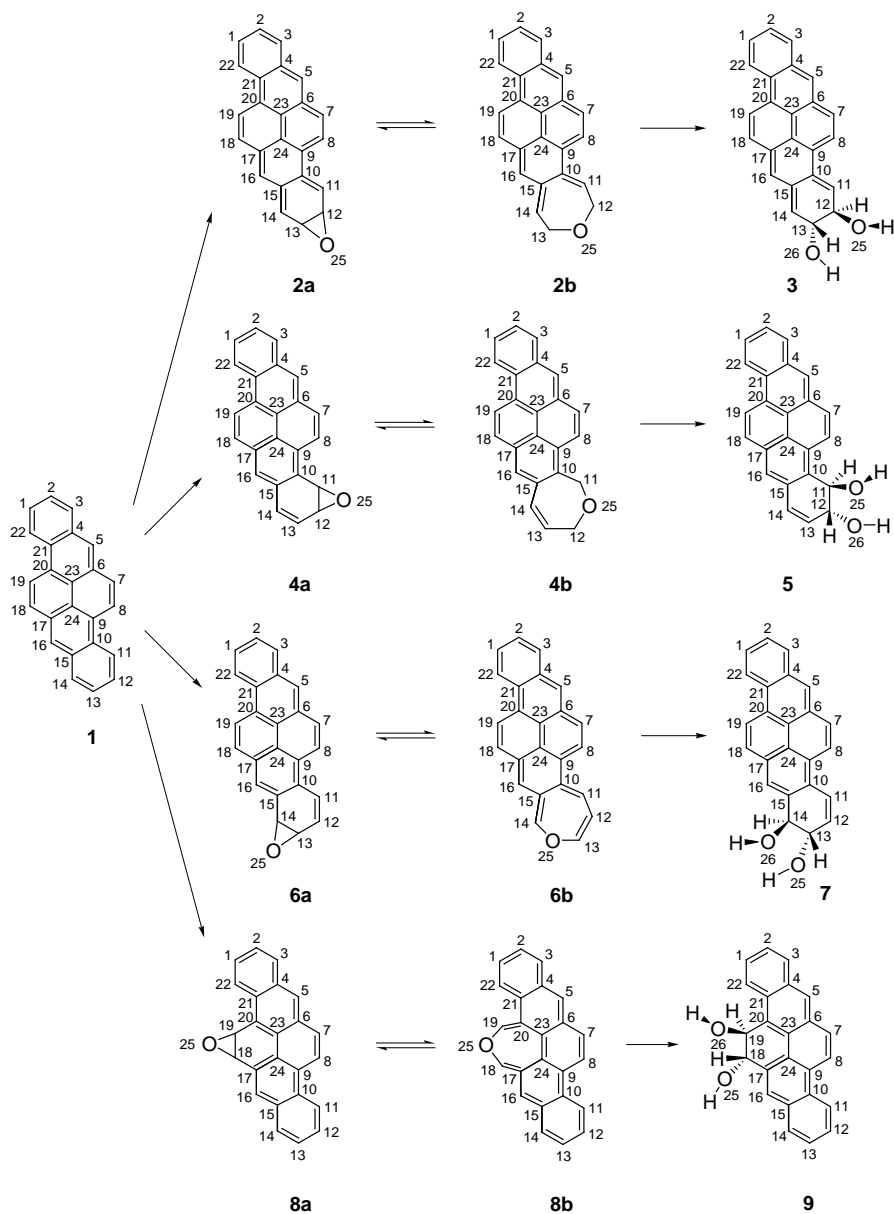
A conformational study of energies and geometries of stable compounds obtained from dibenzo[*a,h*]pyrene by enzymatic treatment with oxygen was carried out using the semiempirical AM1 quantum mechanical method. The energies of possible isomers are strongly dependent on the position occupied by the oxygen atom in the epoxides obtained from dibenzo[*a,h*]pyrene.

Keywords: Oxidations; Dibenzo[*a,h*]pyrene; Dibenzo[*a,h*]pyrene epoxides; AM1 calculations; Semiempirical methods; Carcinogens.

It is well known that certain metacyclophanes can be transformed into pyrene¹ or benzopyrenes², and that planarity is considerably increased in such transformations^{3,4}. The benzo[*a*]pyrene molecule has been studied in many experimental works with a view of characterizing its biological activity^{5,6} and of determining certain aspects related to its reactivity. In this sense, the carcinogenic nature of this compound is striking, when compared with the non-carcinogenic activity of benzo[*e*]pyrene⁷.

Of the experimental procedures dealing with this type of compounds, the enzymatic treatment of benzopyrenes carried out by Boyd⁸ is outstanding. In this reaction, the compound provides different epoxides, depending on the position at which the oxygen atom is attached at the periphery of the benzopyrene molecule. These epoxides are then converted by hydrolysis into *trans* dialcohols in different ratios.

In the present work we report on a theoretical study of transformations of dibenzo[*a,h*]pyrene into epoxides and later into *trans* dialcohols in order to find which of the possible epoxides formed is more stable. This information is used to determine which of the dialcohols would be formed preferentially. To do so, we used a quantum mechanical method to determine the molecular structure of the compounds participating in the process and their relative stability. Scheme 1 shows all the molecules studied.



SCHEME 1

CALCULATIONS

A semiempirical AM1 method was used as it is contained in the MOPAC (ref.⁹) program package. The method is parametrized to reproduce certain experimental magnitudes as well as possible. The AM1 method¹⁰ allows one to calculate satisfactorily heats of formation, molecular geometries, dipole moments and force constants.

In all energy minimizations¹¹, we started from flat hydrocarbon skeletons, assuming bond distances and angles typical of aromatic hydrocarbons. No geometry restriction was accepted. The optimum geometry was calculated by assuming that the molecules are isolated in the gas phase at a temperature of 298.15 K.

RESULTS AND DISCUSSION

The calculated optimum geometries deserve a special analysis because of their relation to planarity and charge distribution discussed below.

*Dibenzo[*a,h*]pyrene*

In dibenzo[*a,h*]pyrene, the starting distance was 1.40 Å for all the C–C bonds and the angles were assumed to be 120°. The calculated structure is planar, in agreement with the experimental findings on this family of molecules^{12,13}. It should be stressed that the greatest diatropism was obtained in the rings formed by atoms 6-7-8-9-24-23 and 17-18-19-20-23-24. The other C–C bonds showed deviations from 1.40 Å less than 0.03 Å. With respect to bond angles, the deviations from 120° were smaller than 2.2°. The molecule has C_2 symmetry and it is flat. The heat of formation is 109.2 kcal/mol.

Epoxides

When treated with oxygen dibenzo[*a,h*]pyrene gives rise to different epoxides whose nature depends on the position of oxygen. The calculated C–C bond lengths correspond to the structure of dibenzo[*a,h*]pyrene, with the exception of the bonds between the carbon atoms bound to the oxygen atom and the distances of adjacent atoms, which are much greater than those obtained for dibenzo[*a,h*]pyrene (see Table I). The C–C distance of the carbons bound to the oxygen is by 0.14 Å longer than in dibenzo[*a,h*]pyrene in molecules of **4a**, **6** and **8a**. However, this difference is less pronounced for this C–C bond in molecule of **2a** (0.09 Å). The bond

TABLE I
AM1 bond lengths in dibenzo[*a,h*]pyrene and epoxides **2**, **4**, **6** and **8**

Bond	Bond length, Å				
	1	2	4	6	8
1-2	1.417	1.421	1.414	1.414	1.412
2-3	1.370	1.366	1.372	1.372	1.375
4-5	1.411	1.403	1.418	1.417	1.423
5-6	1.384	1.393	1.378	1.379	1.370
6-7	1.439	1.432	1.443	1.442	1.473
7-8	1.355	1.361	1.352	1.352	1.494
8-9	1.440	1.432	1.445	1.445	1.475
9-24	1.409	1.391	1.425	1.425	1.404
10-15	1.422	1.466	1.417	1.419	1.425
11-12	1.372	1.460	1.503	1.345	1.368
12-13	1.417	1.516	1.468	1.467	1.422
13-14	1.370	1.457	1.343	1.501	1.366
14-15	1.426	1.364	1.455	1.476	1.430
15-16	1.411	1.443	1.393	1.387	1.403
16-17	1.384	1.361	1.403	1.404	1.392
17-18	1.439	1.446	1.432	1.431	1.436
18-19	1.355	1.350	1.361	1.361	1.356
19-20	1.440	1.446	1.434	1.433	1.437
20-21	1.426	1.417	1.432	1.432	1.437
21-4	1.422	1.427	1.420	1.420	1.417
1-22	1.372	1.368	1.374	1.374	1.376
22-21	1.426	1.431	1.422	1.423	1.421
29-20	1.409	1.413	1.408	1.409	1.404
13-25		1.439			
11-25			1.439		
14-25				1.439	
19-25					1.440

lengths of the atoms adjacent to this bond are about 0.04 Å longer than in dibenzo[*a,h*]pyrene.

The C–O–C angle merits special attention since while in molecule of **8a** there is an angle of 62.5°, angles of 63.6, 62.9 and 62.8° were calculated for molecules of **2a**, **4a** and **6a**, respectively (see Table II). Molecule **8a** is closer to the experimental values observed for molecules of this type¹⁴.

The results obtained with the AM1 method lead to an almost flat structure where all the carbon atoms lie almost in the same plane, with deviations not exceeding 3°. The hydrogens on carbons bound to the oxygen and the oxygen are those lying most outside the plane, as may be seen in Table II. This table presents only the most significant angles. The oxygen forms a semi-envelope with a pseudo-axial pseudo-equatorial orientation. These results concur with the calculations on the smallest molecules of the series^{15,16}.

Regarding the charge located at the oxygen, all the isomers gave similar values (about 0.008 elementary charge units difference between isomers). For isomers **2a** and **8a**, the same charge distribution is obtained for the carbons attached to the oxygen while for isomers **4a** and **6a** the charge located at the adjacent carbons is different. This observation could be attributed to the position occupied by the oxygen in molecules of **2a** and **8a** as compared with the position it occupies in compounds **4a** and **6a**. The values obtained for the oxygen are 0.23 elementary charge units for molecule of **2a**, slightly lower than those calculated for other molecules (0.24 for molecule of **4a** and 0.24 for molecules of **6a** and **8a**). Moreover, no polarization occurs in the carbons bound to the oxygen; rather it is shared by all the carbons.

The calculated heats of formation are presented in Table III. The isomer with the lowest energy is **8a**. It is more stable than **2a**, **4a** and **6a** by 23.3, 4.2 and 4.4 kcal/mol, respectively, in agreement with the known experimental data¹⁷.

The dipole moment calculated for isomer **8a** is lower than that of the other isomers studied. The highest dipole moment corresponds to isomer **6a**. Isomers **2a** and **4a** have values inbetween the dipole moment of **2a** being slightly lower than that of **4a**. The fact that molecules of **8a** and **2a** have the lowest dipole moments can be attributed to the position of by the oxygen and low polarization.

Finally, the experimental results obtained on epoxides confirm the existence of an equilibrium between the oxirenes and oxepines due to the effect of heat or due to radiation. However, the experimental evidence by

TABLE II
AM1 bond and dihedral angles in dibenzo[*a,h*]pyrene and epoxides **2**, **4**, **6** and **8**

Bond and dihedral angles	Values of bond and dihedral angles, °				
	1	2	4	6	8
22-1-2	120.6	120.6	120.5	120.5	120.6
1-2-3	119.9	119.9	119.8	119.8	119.8
4-5-6	120.9	120.9	121.0	121.0	121.0
21-4-5	120.0	120.0	120.0	120.0	119.5
5-6-7	121.4	121.4	121.5	121.5	119.5
6-7-8	121.5	121.1	121.7	121.7	119.0
7-8-9	121.6	121.3	121.7	121.9	119.2
8-9-24	118.3	118.8	117.9	117.6	119.4
10-15-16	120.0	118.5	120.0	120.8	119.5
11-12-13	120.5	117.4	117.8	121.8	120.6
12-13-14	119.9	116.6	121.0	117.1	120.0
13-14-15	120.8	122.1	122.8	118.8	120.7
14-15-16	120.3	120.0	119.4	118.8	120.9
15-16-17	120.9	122.0	120.8	120.6	121.0
16-17-18	121.5	121.6	121.4	121.3	120.5
17-18-19	121.5	121.8	121.1	121.1	121.2
18-19-20	121.6	121.9	121.5	121.4	121.4
19-20-21	121.8	121.8	121.9	121.8	120.7
20-21-4	119.2	119.3	119.2	119.2	119.2
22-21-4	117.9	117.7	118.0	118.0	117.9
1-22-21	121.3	120.6	121.2	121.2	121.1
29-20-21	120.0	120.1	119.8	119.8	120.3
25-13-14		116.9			
25-11-10			116.8		
25-14-15				116.7	
25-19-20					117.3
14-15-16-17	0.	176.	179.	180.	179.
13-14-15-16	0.	179.	182.	177.	-179.
12-13-14-15	0.	6.	0.	0.	0.
11-12-13-14	0.	359.	0.	2.	-1.
24-17-18-19	0.	2.	2.	359.	3.
25-13-14-15		117.			
25-11-10-9			247.		
25-14-15-16				243.	
25-18-17-16					113.

Agarwal¹⁷ indicates that the transformation occurs only through an epoxide.

The present study also includes the data on oxepines to give an idea of possible intermediate processes of the reaction. Calculated heats of formation of these oxepines predict a lower stability than that of the corresponding oxirenes (see Table III) except isomer **2b**.

Isomers **2b** and **8b** show the strongest differences with respect to stability. Thus, whereas epoxide **8a** is more stable than other epoxides, the corresponding oxepine is more unstable than other oxepines. The opposite occurs in the case of **2b** since whereas the epoxide is more unstable, the oxepines is more stable. Moreover, isomers **4b** and **6b** have higher heats of formation (though almost identical) than the corresponding epoxides.

At this point it seems necessary to make a more specific note on epoxides. Epoxide formation involves breakage of an sp^3 bond of the oxepine with the concomitant transformation of a six-membered carbon ring fused to a three-membered oxygen ring into a seven-membered oxygen ring. The three-membered ring must be subject to considerable strain, which disappears when it is converted into a seven-membered one. This situation should give rise to greater stability in the system due to both a higher degree of aromaticity and to the strain release, although this was not confirmed in all the molecules studied. For example, in the case of compound **2b**, the stability of the oxepine is greater than that of the epoxide, confirming the above statement. However, this evidence does not apply to oxepine **8b** which is less stable than the corresponding epoxide. Other two epoxides, **4a** and **6a**, are close in their stabilities, but they both are slightly more stable than the oxepines. An explanation for this can be found in the

TABLE III
AM1 heats of formation of epoxides and oxepines

Compound	$\Delta H_{f,298}^0$, kcal mol ⁻¹	
	epoxide	oxepine
2	125.4	96.1
4	106.4	116.3
6	106.6	116.3
8	102.1	136.9

position of oxygen in the seven-membered ring. Thus, in the epoxide derived from **8a**, the seven-membered ring has C(17), C(24), C(29), C(20) carbons bound to other rings, which would prevent the forming angles from being equal to those that might arise if one were dealing with a seven-membered ring without any type of impediment. Accordingly, it must be subject to more stretching than the other molecules studied. In molecules **2a**, **4a** and **6a**, the seven-membered ring is bound to the other rings only by the C(10)–C(15) bond, thus helping it to form a seven-membered ring subject to less stretching. In addition, the molecule of epoxide **2a** is more aromatic than those of **4a** and **6a** due to the distribution of the π -electron cloud in **2a**. This is because of a higher symmetry of **2a** and also because of a longer C–O bond and shorter C–C bond in **2a**, compared to **4a** and **6a**.

In all cases, the oxepines obtained from **2a**, **4a**, **6a** and **8a** become less flat as the seven-membered ring is being formed. Likewise, **8b** departs from planarity because the strain in the seven-membered ring is greater than in other oxepines, as explained above. Distortion of the planar ring also affects the resonance energy of the molecule and contributes to a lower stability of **8b**. The difference in the heat of formation between the oxepines and the epoxide in the pairs of **4a–4b** and **6a–6b** is lower than 10 kcal/mol. This relatively small difference explains satisfactorily the interconversion between them and the fact that the corresponding alcohol can be obtained from both of them. With interconversions **2a–2b** and **7a–7b**, the energy difference is greater, which indicates that the interconversion does occur but not as easily as in the previous cases. These results would also confirm the experimental observation of interconversion between the oxepines and the corresponding epoxide. The greater energy content of the oxepines in **4b**, **6b** and **8b** explains why heat is necessary for an equilibrium between these compounds and the experimental fact that hydrolysis always occurs through the epoxide. Accordingly, this compound may be an intermediate through which the reaction occurs.

Alcohols

Hydrolysis of each of the epoxides gives rise to two conformers of the same dialcohol. The two conformers of this dialcohol differ in the orientation of the OH group in the molecule. The carbon skeleton in these structures is almost flat. Heats of formation for each isomer are presented in Table IV. From the two conformers of **9**, that one with a pseudo-axial orientation (**9a**) is more stable. The other one (**9b**) is less stable than the two conform-

ers of **7**, and the difference in the heat of formation between **9a** and **9b** is greater than with the two conformers of the other dialcohols. With **3** and **7**, this difference is very small.

TABLE IV
AM1 heats of formation of *trans* dialcohols

Compound	$\Delta H_{f,298}^0$, kcal mol ⁻¹	
	pseudo-axial	pseudo-equatorial
3	28.3	28.4
5	8.7	10.4
7	7.5	7.6
9	4.4	8.5

CONCLUSIONS

All the compounds studied are almost planar. In view of the results obtained, the most probable reaction path is through **8a** and **9a**. Although the epoxide prefers a pseudo-axial orientation, hydrolysis of this compound yields two possible orientations, pseudo-axial and pseudo-equatorial.

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