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Oxidation of Dibenzo[*a*,*e*]fluoranthene by Osmium Tetroxide

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Dibenzo[*a*,*e*]fluoranthene is treated by osmium tetroxide, the nature, structure, and configuration of the compound obtained (a *trans* dihydro diol) are defined taking into account the chemical, theoretical, and physicochemical arguments.

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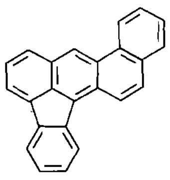
On traite le dibenzo[*a*,*e*]fluoranthène par le tétroxyde d'osmium; on définit la nature, la structure et la configuration du composé obtenu (un dihydro diol *trans*) en tenant compte d'arguments chimiques, théoriques et physicochimiques. [Traduit par le journal]

Recently we presented a preliminary note (1) on the properties of dibenzo[*a*,l]pyrene (**1**) and dibenzo[*a*,*e*]fluoranthene (**2**). The fact that the hydrocarbon **2** is strongly cancerogenic has been confirmed by recent experiments (2) achieved with a product whose structure has no ambiguity.



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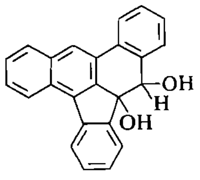

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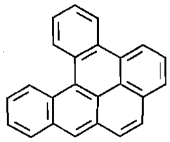

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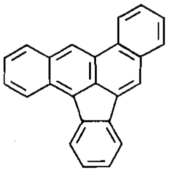

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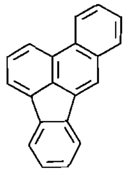

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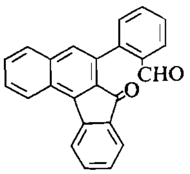

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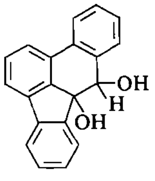
We must note that contrary to **1** this molecule does not seem to possess a geometric region corresponding to the definition of the "K zone" following the terminology of Pullman and Pullman (3). Consequently, it was interesting to submit it to the action of osmium tetroxide in order to determine the presence of a bond with a marked ethylenic character of the K zone type (4).

The first observation that we have made relates to the slowness of the reaction between **2** and osmic anhydride. In fact, contrary to the majority of the cases described in the literature for the series of benzo[*a*]anthracene (5) the time of contact to obtain an appreciable quantity of the complex had to be extended to 40 days. (Note: the action on the lower homolog **3** is not easier since in this case, the reaction must be continued for several months.) On the other hand, the oxidation of the isomer (**4**), or naphto[2,1-*b*]fluoranthene, which has been studied equally from the theoretical and spectroscopic points of view, occurs in a very short period of time.

These operations were carried out using the method of Criegee *et al.* (6) modified by Cook and Schoental (5). After dissociation of the complex, treatment, and chromatography, we have isolated a compound which is proved, as we expected, to be a dihydrodiol. This is confirmed by the mass spectrum, the microanalysis, and the infrared spectrum. For the position of the reactive bond, a chemical proof as well as the examination of the n.m.r. spectra allowed us to conclude that the two OH groups were situated on the carbons 5 and 5*a* and from this fact, that the diol corresponds to formula **5**. Indeed, from the chemical point of view, the oxidation by lead tetraacetate (7) breaking the 5–5*a* bond, leads to (formyl-2-phenyl)benzo[*c*]-fluorenone (**6**), the structure of which is defined without ambiguity by the resonance spectra of the protons, microanalysis, and fragmentation in mass spectrometry.

Confirmation of this structure was obtained by the complete analysis of the resonance spectrum of aromatic protons of both the diol and the parent hydrocarbon which confidently identifies all the protons of the molecules. Furthermore, the n.m.r. analysis provided information on the conformation of the diol obtained. Thus, it appears that the mechanism of reaction of osmium tetroxide with aromatic hydrocarbons parallels closely that established for reactions with aliphatic or cycloaliphatic compounds. Then, the diols formed by the action of osmium tetroxide should have a *cis* conformation (6) and only in the course of biochemical degradation could *trans* diols be formed directly from the hydrocarbons (8).

However, we have been somewhat surprised to be unable to obtain the cleavage of **5** in benzofluorenone (**6**) by sodium periodate, a specific reactive for the oxidation of *cis* glycols; and for this operation, to have to use lead tetraacetate with which the cleavage occurs very easily. Since the same phenomenon was observed for the oxidation into (formyl-2-phenyl)-1-fluorenone (**8**) of the diol **7** obtained from the lower homolog **3** of the hydrocarbon **2**, this observation suggested a *trans* conformation for these glycols.



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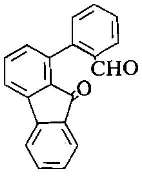

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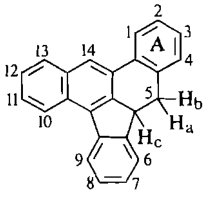
This assumption was further supported by a comparative examination of the spectra of diol **5** in the infrared taken in the solid state in KBr (bands OH, 3280 and 3370 cm^{-1}) and in solution in CS_2 (bands OH, 3550 and 3580 cm^{-1}). The shift of the characteristic bands, that we also find in the spectrum of diol **8** (KBr, 3300 cm^{-1}; CS_2, 3670 and 3550 cm^{-1}; $CHCl_3$, 3670 and 3550 cm^{-1}), does not appear consistent with the intramolecular hydrogen bond usually present in the *cis diols* (9). The variations observed suggest that the two OH groups are at a distance from each other, and thus situated on each side of the molecule midplane.

These indirect chemical and spectroscopic observations do not constitute unquestionable evidence of the *trans* type configuration. Direct evidence from the n.m.r. spectrum is not available since only one proton is directly bonded to the hydrocarbon framework and since no observable coupling between the hydroxylic protons is present.

For this reason, dihydro-5,5*a*-dibenzo[*a*,*e*]-fluoranthene (**9**) was prepared by the method of Vingiello and Youssef (10) and its n.m.r.



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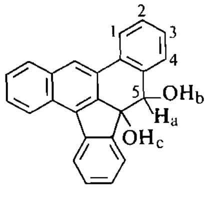

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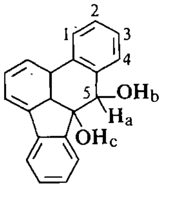

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spectrum was analyzed and compared with that of the two diols **5** and **7**.

The spectrum of the dihydrogenated compound **9** exhibits three aliphatic protons (designated as a, b, and c in the formula) characterized by their chemical shifts and their coupling constants (δ (p.p.m.): $H_a = 4.09$, $H_b = 2.67$, $H_c = 3.56$; $J_{ab} = 14.5$ Hz, $J_{bc} = 14.3$ Hz, $J_{ac} = 6$ Hz). Thus, the high field proton H_b should be geminal and strictly *trans* with respect to the two others. Indeed, a large vicinal coupling could arise only from a strict *cis* or *trans* configuration, but the former one with a zero dihedral angle is sterically impossible in a cyclohexane type structure. Finally, the smallest coupling corresponds to a vicinal *gauche* interaction.

The assignment of H_a and H_c is easily made by double resonance experiments because in the lower field one H_a exhibits a coupling of 0.8 Hz with the neighbor aromatic H_4 proton and even a smaller long distance coupling with H_2 (*ca.* 0.5 Hz). On the other hand, the H_c resonances are very little broadened, but still exhibit an unresolved coupling with the H_6 proton. On the contrary, the high field resonances of H_b exhibit only very little, if any, coupling with H_4.

In the diol compounds **5** and **7** the remaining proton appears at 4.925 and 4.920 p.p.m. respectively. The decoupling experiments confirmed that the corresponding lines had the same structure, due to long distance coupling to H_4 (0.9 Hz) and H_2 (0.5 Hz), as H_a. Consequently, H_b and H_c have been substituted by hydroxylic groups, in agreement with the assumed *trans* configuration.

The H_a proton exhibits a downfield shift of 0.83 p.p.m. upon diol substitution. This shift could appear small when compared to downfield shifts of about 2 p.p.m. of geminal protons in cyclohexanol, but it does not correspond to the simple effect of the geminal OH group. As a matter of fact, the H_a proton has a more marked equatorial character in the dihydrogenated compound **9** than in the diol, resulting in a lowfield shift due to steric repulsion with H_4. Indeed, the $J_{H_a-H_c}$ coupling, in compound **9**, is nearly a *gauche* coupling, but the $J_{H_a-OH_b}$ coupling (11.4 Hz) certainly corresponds to a more widely opened geminal angle. Thus, the H_a proton is probably displaced a little further from the molecular plane, resulting in less steric interaction with H_4.

Considering the importance of this conclusion of a *trans* diol configuration with respect to the assumed mechanism of the diol formation and to the problems of the metabolism and cancerogenic activity of these compounds, a systematic n.m.r. investigation of the configuration of the diols obtained by osmium tetroxide and *o*-quinone reduction from related hydrocarbons possessing a true "K zone", has been undertaken. These results, which will be reported in detail elsewhere (11), indicate that the behavior of dibenzofluoranthene (**2**) with respect to osmium tetroxide is not at all an exception due to some steric or electronic reasons but is a common rule. As a matter of fact, *trans* diols, which could often be assigned by n.m.r. much more easily because of high symmetry and vicinal HH couplings, have been found for any aromatic hydrocarbon treated by osmium tetroxide, in contrast with the diols obtained by reduction of quinone which correspond to a *trans* H structure. No direct evidence for *cis* diols has been yet found, contrary to the structure assumed until now. For example, the unsymmetrical diol **10** exhibits a vicinal coupling $J_{H_a-H_d}$ of 3.9 Hz corresponding to a *gauche* configuration, which could be attributed to a *cis* configuration, but could correspond as well to two equatorial protons as revealed by the detailed analysis of the n.m.r. spectrum of the whole molecule.

But, in spite of its importance, this question was not the purpose of this work and the

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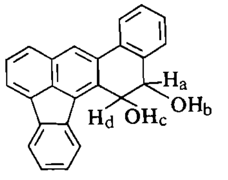

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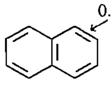
problem, presently under active investigation, will be reported and discussed later (11) from the point of view of the n.m.r. analysis as well as that of its chemical aspects with respect to previous assignments.

In regard to dibenzofluoranthene, chemical investigations, such as the possible diol conversion, are continuing in order to obtain a chemical proof of this structural assignment, more specific than the unsuccessful periodate oxidation. It is, however, worthwhile to mention that we were not able to obtain the corresponding epoxide until now.

In conjunction with these practical results, the prediction of the eventual reactive zone has been undertaken by the theoretical calculation of the bond indices of the hydrocarbons **2** and **4**.

We know that naphthalene (**11**), anthracene (**12**), and benzanthracene (**13**) react with osmium tetroxide uniquely on the bond possessing the strongest ethylenic character and therefore the greatest bond order, the reaction being faster the higher the bond order. Using the method of Pariser, Parr, and Pople (12) we obtain for these hydrocarbons the three values indicated in the formulas and which agree well with the experimental results.



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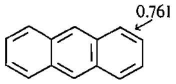

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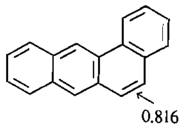

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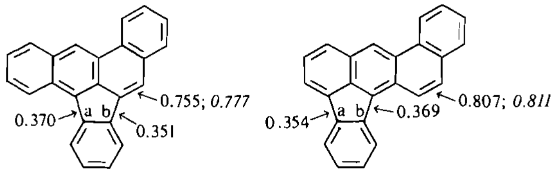
For the hydrocarbons **2** and **4** and assuming all the bonds of equal length ($\beta = -2.39$ eV) an analogous calculation leads to the values indicated in Fig. 1.

The indices of 0.755 for **2** and 0.807 for **4** which are the highest for each molecule could thus appear satisfactory since they situate the attack at the position where it does occur.

Nevertheless, the chosen parameters for the two molecules do not allow us to obtain a correct description of the electronic absorption spectrum, the "theoretical" spectrum being displaced too much towards the visible.



2 **4**

FIG. 1. Calculated bond orders for hydrocarbons **2** and **4**.

Thus it appears necessary to make the preceding calculation more precise by taking the values of β (thus the bond length) different from the rest of the molecule for the bonds a and b of Fig. 1. This value of β has been deduced by interpolation of the values (Table 1) used by Mulliken and Parr (13) for butadiene and benzene.

TABLE 1. Values for β used for butadiene and benzene (13)

Bond	Length (Å)	β (eV)	Index *p*
C1—C2 butadiene	1.34	−2.92	0.977
C2—C3 butadiene	1.46	−1.68	0.212
Benzenic	1.39	−2.39	0.666

This leads to a mean value $\beta_a = \beta_b = -1.90$ eV and a bond index $p_a = p_b = 0.360$. With this new parameter we then obtain the values of *0.777* and *0.811* respectively for the bond orders C5—C5*a* of **2** and C5—C6 of **4** (Fig. 1) which thus preserve the strongest character of a double bond.

Likewise this same value of mean *B* obtains the best correlation between the theoretical and experimental spectra of the two hydrocarbons (Table 2).

The u.v. absorption spectra of the compounds **2** (Fig. 2) and **4** (Fig. 3) show strong analogies between them and yet are clearly distinguishable from that of benzanthracene (14) and from phenyl benzanthracene (Fig. 4). The latter presents all the characteristics of the tetraphenic series: band α forbidden, bands p, β, and β′ permitted. On the other hand, the relative intensities of the various bands bring the hydrocarbons **2** and **4** nearer to the fluoranthenes for which the electronic spectra presents the

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TABLE 2. Comparison of theoretical and experimental spectra for compounds **2** and **4**

Band	Spectrum	
	Theoretical	Experimental
Hydrocarbon **2**		
p	382.6	390
α	384	Band masked
β	320	330
Hydrocarbon **4**		
p	372.9	380
α	348.9	Band masked
β	325.5	325

following structure: band p permitted, band α forbidden, bands β and β′ permitted.

The absorption spectra confirm a convenient choice of parameters and consequently constitute a nonnegligible proof of the validity of theoretical calculation of the bond orders of dibenzo[*a*,*e*]fluoranthene. These calculations have been confirmed by the chemical results.

Thus the low relative value of 0.777 for the reactive bond order, possibly associated with the steric requirements, could explain the slowness of the attack by osmium tetroxide. This appears more correct especially as the same calculation applied to benzofluoranthene (**3**) leads to an index of 0.767, appreciably lower, for the bond involved in the reaction. Now we have effectively established that this hydrocarbon reacts even more slowly than its superior homolog.

When the biological results concerning the hydrocarbons **2** and **4**, their benzologs, and nitrogenous analogs are published, we propose to continue our investigations and to extend them to other cancerogenic hydrocarbons apparently lacking in the K zone that present the family of more condensed homologs of fluoranthene.

Experimental

The melting points were determined either in a capillary tube on a Buchi apparatus or on a metallic block heated electrically and with an electronic temperature detection (laboratory built apparatus).

The centesimal analyses were made by the Laboratoire de Microanalyse du C.N.R.S. at Gif-sur-Yvette.

The u.v. spectra in hexane have been read on a spectrophotometer Safas 1800 modified by the laboratory, and the i.r. spectra, on a KBr disk and in solution in CS_2, on a Perkin–Elmer 225 apparatus.

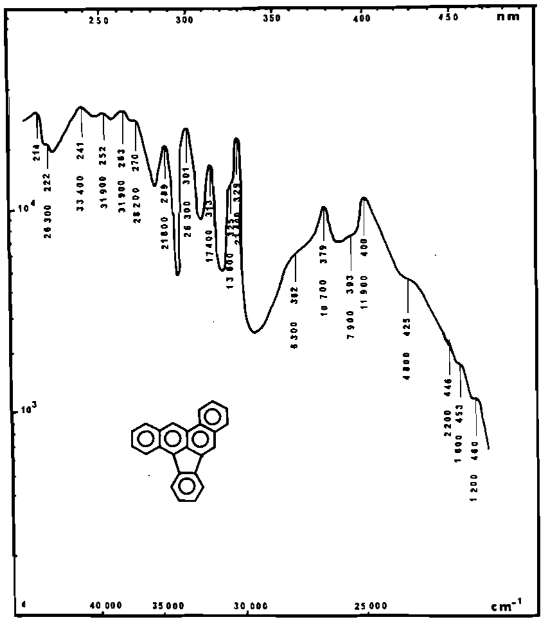

FIG. 2. Ultraviolet spectra of **2**.

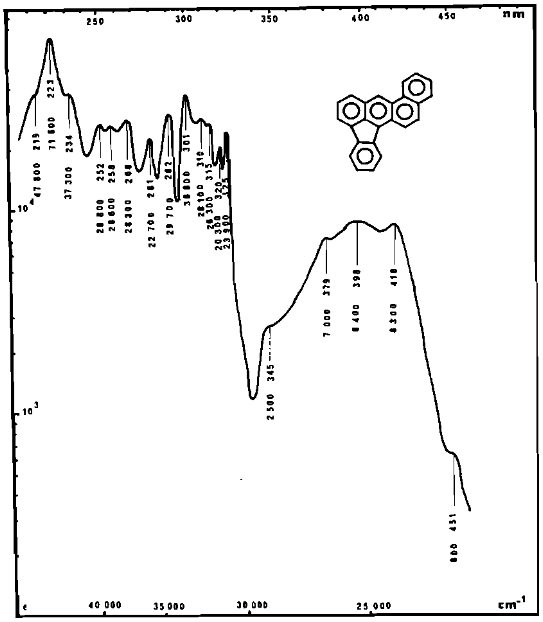

FIG. 3. Ultraviolet spectra of **4**.

The n.m.r. spectra at 100 MHz, have been recorded at high resolution in a 10 mm diameter cell on a Varian XL 100 machine at 34 °C. The concentrations of solutions in $CDCl_3$ were from 1 to 3 × 10^{-2} *M*.

The protons were identified by selective decoupling, tickling, and INDOR. Using chloroform as internal reference, the values of chemical displacement (*d*) indicated in p.p.m. have been converted to TMS taking *d*($CHCl_3$) = 7.26 p.p.m.

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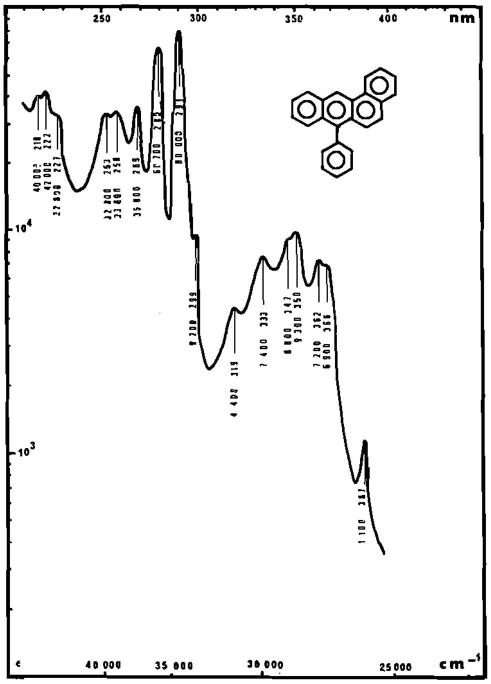

FIG. 4. Ultraviolet spectra of phenyl benzanthrene.

Oxidation by Osmium Tetroxide

The technique used for the three hydrocarbons **2**, **3**, and **4** is that designed by Cook and Schoental (5).

5,5a-Dihydroxy-5,5a-dihydrodibenzo[a,e]fluoranthene (5)

The solution of 1.2 g of dibenzofluoranthene (**2**), 1 g of osmium tetroxide, and 790 mg of pyridine in 120 ml of dry benzene is maintained at 30° for 3 to 4 weeks. Then the brown solution is decanted and the solid brown complex is dissolved in a minimum of methylene chloride. This solution is agitated and treated with an equivalent volume of an aqueous solution of potassium hydroxide (2%) and mannitol (10%). The operation is repeated several times until the aqueous phase is colorless. The organic phase is washed with water, dried with Na_2SO_4, and the solvent is evaporated under vacuum. The recrystallization in benzene of the solid obtained gives 540 mg of fine colorless needles, m.p. (inst.) 224–225° (slow decomposition from 195°); n.m.r.: δ p.p.m.: $H_a = 4.925$, $H_b = 2.95$, $H_c = 2.23$, $H_1 = 8.21$, H_2 and $H_3 = 7.425$ to 7.465, $H_4 = 7.90$, H_6, H_9, and $H_{13} = 7.92$ to 8.01, H_7 and $H_8 = 7.425$ to 7.465, $H_{10} = 8.56$, H_{11} and $H_{12} = 7.575$, $H_{14} = 8.04$; $J_{H_a-H_b}$ (H, OH) = 11.4 Hz; $J_{H_a-H_c} \simeq 0.5$ Hz, $J_{H_b-H_c} \simeq 0$.

Anal. Calcd. for $C_{24}H_{16}O_2$ (mol. wt. 336); C, 85.70; H, 4.80; O, 9.51. Found (336, mass spectrum): C, 84.55; H, 4.85; O, 9.21.

The treatment of the reactive benzene solution with mannitol and potassium hydroxide permits the recovery of 460 mg of the initial hydrocarbon.

A second test using double the quantity of osmium tetroxide under the same conditions yielded 730 mg of recrystallized dihydrodiol. The hydrocarbon–dihydrodiol mixture from the treatment of the mother liquors can be separated on an alumina column eluted with benzene for the hydrocarbon and then with chloroform for the diol.

5,5a-Dihydroxy-5,5a-dihydrobenzo[b]fluoranthene (7)

The above technique, with an equivalent of osmium tetroxide, starting with 500 mg of benzo[*b*]fluoranthene (**3**) and after a time of contact of 3 months, leads to the recovery of 250 mg of hydrocarbon and of 130 mg of dihydrodiol recrystallized in benzene into brilliant, colorless needles, m.p. (inst.) 242–243° (decomposition from 215°). n.m.r.: δ p.p.m.: $H_a = 4.92$, $H_b = 2.90$, $H_c = 2.165$; $J_{H_a-H_b} = 11.4$ Hz, $J_{H_a-H_c} = 0.8$ Hz, $J_{H_b-H_c} \simeq 0$. Very complex spectrum of aromatic protons, $H_1 = 7.92$, H_2, H_3, H_7, and $H_8 \simeq 7.42$, $H_4 = 7.69$, H_6 and $H_9 = 7.72$ and 7.84, H_{10}, H_{11}, and $H_{12} \simeq 7.52$.

Anal. Calcd. for $C_{20}H_{14}O_2$ (mol. wt. 286): C, 83.89; H, 4.93. Found: C, 83.59; H, 4.84.

5,6-Dihydroxy-5,6-dihydronaphtho[2,1-a]fluoranthene (10)

With the naphtho[2,1-*a*]fluoranthene (**4**) and an equimolar quantity of osmic anhydride, the reaction is completed after 48 h. The hydrocarbon (310 mg) gave 210 mg of fine colorless needles of diol (**10**) after recrystallization in benzene, m.p. (inst.) 194–195° (decomposition from 180°); n.m.r.: only the glycolic part of the spectrum has been analyzed; δ p.p.m.: $H_a (H_5) = 5.02$, $H_b (OH_5) = 2.82$, $H_c (OH_6) = 1.98$, $H_d (H_6) = 5.77$; $J_{H_a-H_b} = 10.3$ Hz, $J_{H_c-H_d} = 7.0$ Hz, $J_{H_a-H_d} = 3.9$ Hz.

Anal. Calcd. for $C_{24}H_{16}O_2$ (mol. wt. 336): C, 85.70; H, 4.80. Found: C, 84.23; H, 4.96.

(Formyl-2-phenyl)-6-benzo[c]fluorenone (6)

All the attempts to produce oxidative cleavage of the diol **5** by metaperiodate by the described methods (15, 16) at different conditions of temperature and p*H*, have led only to the recovery of the initial product.

On the other hand, oxidation by lead tetraacetate using the technique of Boyland and Wolf (7) occurs very easily. The mixture of 350 mg of diol **5** and 1 g of lead tetraacetate in 100 ml of benzene is agitated at room temperature. After 3 h the chromatography of a sample on a thin layer of silica shows the disappearance of the initial product and the presence of a single compound (orange spot). The benzene solution is then filtered, washed successively with 1 *N* hydrochloric acid, with an aqueous solution of Na_2CO_3, then with water. After drying on Na_2SO_4 the solvent is evaporated under vacuum. The reddish residue is chromatographed on a silica column. The elution of a dark red ring by benzene, after evaporation of the solvent, gives fluorenone (**6**) the recrystallization of which in ethanol produces 290 mg of orange prismatic needles, m.p. 217–218°. Mass spectrum: molecular peak at 334, important peak at 305 by loss of —CHO; n.m.r. (The protons are numbered keeping the numbering of the diol or the hydrocarbon.): H_5(CHO) = 9.92 (coupling 0.7 Hz characteristic of the *ortho* substituted benzaldehydes), H_1, H_2, H_3, H_4 (phenyl) = 7.51 to 7.66, H_6 and $H_9 = 8.075$ and 8.12, H_7 and $H_8 = 7.38$, $H_{10} = 8.61$, H_{11} and $H_{12} = 7.69$, $H_{13} = 7.895$, $H_{14} = 7.63$.

Anal. Calcd. for $C_{24}H_{14}O_2$ (mol. wt. 334): C, 86.21; H, 4.23; O, 9.57. Found: C, 86.52; H, 4.50; O, 9.69.

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(Formyl-2-phenyl)-1-fluorenone (8)

Same technique as previously cited for diol **7**. Test with periodate negative. The product recrystallizes from the benzene – petroleum ether mixture in yellow crystals, m.p. 108–109°.

Anal. Calcd. for $C_{20}H_{12}O_2$ (mol. wt. 284): C, 84.48; H, 4.26. Found: C, 83.82; H, 4.39.

5,5a-Dihydrodibenzo(a–e)fluoranthene (9)

This hydrocarbon was prepared following the method of Vingiello and Youssef (11) with a view to its study in n.m.r. δ p.p.m.: $H_a = 4.09$, $H_b = 2.67$, $H_c = 3.56$; $J_{H_a-H_b} = 14.5$ Hz, $J_{H_a-H_c} = 6$ Hz, $J_{H_b-H_c} = 14.3$ Hz. $H_1 = 8.385$, H_2 and $H_3 = 7.40$ to 7.46, $H_4 = 7.742$, H_6, H_9, and $H_{13} = 8.04$ to 8.08, $H_{10} = 8.68$, H_{11} and $H_{12} = 7.58$, $H_{14} = 8.10$.

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1. O. Perin-Roussel, F. Perin, and P. Jacquignon. Tetrahedron Lett. **14**, 1227 (1974).
2. F. Zajdela et al. To be published.
3. A. Pullman and B. Pullman. Cancérisation par les substances chimiques et structure moléculaire. Masson, Paris, 1955. p. 216.
4. G. M. Badger. J. Chem. Soc. 1809 (1950).
5. J. W. Cook and R. Schoental. J. Chem. Soc. 170 (1948).
6. R. Criegee, B. Marchand, and H. Wannonius. Ann. Chem. **99**, 550 (1942).
7. E. Boyland and G. Wolf. Biochem. J. **47**, 64 (1950).
8. J. N. Daly, D. M. Jerina, and B. Witkop. Experientia, **28**, 1129 (1972).
9. L. P. Kuhn. J. Am. Chem. Soc. **74**, 2492 (1952).
10. F. A. Vingiello and A. K. Youssef. Chem. Commun. **68** (1968).
11. J. M. Lhoste, J. Mispelter, M. Croisy-Delcey, O. Perin-Roussel, F. Perin, and P. Jacquignon. To be published.
12. (*a*) R. Pariser. J. Chem. Phys. **21**, 568 (1953); (*b*) R. G. Parr. Quantum theory of molecular electronic structure. Benjamin, New York. 1964. pp. 240 and 257; (*c*) J. A. Pople. Trans. Faraday Soc. **49**, 1375 (1953).
13. R. S. Mulliken and R. G. Parr. J. Chem. Phys. **19**, 1271 (1951).
14. I. Berenblum, R. Schoental, and E. R. Holiday. Cancer Res. **3**, 689 (1943).
15. M. S. Newman and S. Blum. J. Am. Chem. Soc. **86**, 5598 (1964).
16. H. I. Hadler and A. C. Kryger. J. Org. Chem. **25**, 1896 (1960).