from R = CH_3 to R = n-C_4H_9; the series of saturated carbonols V includes those in which R = CH_3, C_2H_5 and n-C_4H_9; the series of unsaturated carbinols IX includes those in which R = CH_3 and C_2H_5; the series of chromenes VIII includes those in which R = CH_3, C_2H_5 and n-C_4H_9.

MINNEAPOLIS, MINNESOTA
RECEIVED NOVEMBER 15, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Ultraviolet Absorption Spectra of Some Derivatives of 1,2-Benzanthracene

BY R. NORMAN JONES[1]

The ultraviolet absorption spectrum of 1,2-benzanthracene has been measured by Capper and Marsh,[2] by Clar[3] and by Mayneord and Roe.[4] Because of the carcinogenic activity of some of its simple alkyl and ace-derivatives, a large number of such compounds have been synthesized and their chemical and biological behavior investigated in several laboratories.[5,6,7] Since eleven such derivatives complementary to those previously studied were available in this Laboratory it seemed desirable to make a careful study of their absorption spectra.

Experimental Procedure

In this study a Bausch and Lomb Medium Quartz Spectrograph was used in conjunction with a Hilger Spekker Photometer and a hydrogen discharge tube designed by Dr. Hugh H. Darby.[8] Some difficulty was initially found in lining up the spectrograph with a photometer of different manufacture. This was overcome by mounting the photometer on a Hilger "Short Bar," the base support of which was replaced by a specially designed casting underslung from the projecting front platform of the spectrograph and accurately machined to fit the Short Bar. By means of set screws and lock nuts in the casting a lateral variation of about 10° on either side of the optical axis was possible to assist the correct alignment of the photometer and spectrograph. To obtain a sharp image it was found necessary to remove the quartz window from in front of the slit and bring the photometer to within 1 mm. of the slit cover.

The use of a hydrogen discharge tube as a source of continuous ultraviolet light is exceedingly convenient and much to be preferred to the tungsten steel spark. The Darby tube has the advantage over other designs of operating at 15 kilovolts, making it possible to interchange with the tungsten steel spark without alteration of the electrical supply circuit. It also requires no water cooling system. The Spekker photometer needs a point source of light and as the discharge in the hydrogen tube occurs along a 10 cm. capillary tube, the correct alignment of the tube with the photometer is difficult and it is necessary to mount the tube in a precision micrometer stand. Incorrect alignment is indicated by a difference in the intensities of the two spectra with no cells in the light path and the photometer drum set at zero. Once correctly aligned the tube has needed no further attention over a period of six months.

Eastman Process plates were used and developed for four minutes at 20–22° in Eastman high contrast developer (Formula D. 19). They were analyzed by visual spotting of the match points directly on the plate against a suitable uniformly illuminated background and the reading was facilitated by projection onto a ground glass screen.[9] The wave length scale was photographed onto the top and bottom of each plate and was calibrated against the spectrum of a copper spark.

All measurements were made in quartz cells of 1-cm. length with fused ends (Hilger Type H. 292). Absolute alcohol was used as solvent and solutions were prepared by progressive dilution of an initial sample weighed out on a microbalance. Measurements were made with a slit width of 0.12 mm. at 20–25°. The results are calculated in terms of $\log_{10} E_{\text{molar}}$ where $E_{\text{molar}} = \log_{10} I_0/I \cdot 1/cl$.

c = concentration of solute in moles per liter
l = cell length in cm.
$\log_{10} I_0/I$ = extinction coefficient read directly from the photometer drum

By suitable adjustment of the concentration it was possible to take the whole spectrum on four or five plates with thirty-one exposures on each, at the same time making certain that regions where fine structure was present were photographed under conditions of maximum sensitivity ($\log I_0/I > 1$).

Results

1,2-Benzanthracene.—Measurements on 1,2-benzanthracene itself were first made in order to compare the results obtained using this equipment with those of prior investigators. The first measurements of the absorption spectrum of 1,2-benzanthracene were made by Capper and Marsh,[2] whose curve agrees qualitatively in shape with that of the more recent investigators. The intensity

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(1) Commonwealth Fund Fellow.

(2) Capper and Marsh, *J. Chem. Soc.*, 724 (1926).

(3) Clar, *Ber.*, **65**, 503 (1932).

(4) Mayneord and Roe, *Proc. Roy. Soc.* (London), **A152**, 299 (1935); **A158**, 634 (1937).

(5) Fieser, *Am. J. Cancer*, **34**, 37 (1938).

(6) Shear, *ibid.*, **33**, 499 (1938).

(7) Cook, *Ergebnisse der Vitamin- und Hormonforschung*, **2**, 213 (1939).

(8) Private communication.

(9) Rosebury, *Science*, **83**, 86 (1936).

measurements in terms of log *E* are numerically about one log unit too great but the units in which *E* is calculated are not stated. Clar[3] obtained substantially the same curve with intensity measurements of the correct order of magnitude. In Table I are given the wave lengths and intensities of the maxima I obtained together with the values interpolated from the graph of Mayneord and Roe[4] and those of Capper and Marsh (the latter converted from oscillation frequencies to wave lengths).

TABLE I

POSITIONS AND INTENSITIES OF THE MAXIMA OF THE ULTRAVIOLET ABSORPTION SPECTRUM OF 1,2-BENZANTHRACENE

Band[a]	R. N. J.		Mayneord and Roe		Capper and Marsh
A	2540 Å.	(4.56)	2540 Å.	(4.62)	..
B	2655	(4.60)	2660	(4.65)	..
C	2765	(4.85)	2760	(5.00)	..
D	2870	(4.97)	2880	(5.10)	2875
E	2995	(3.99)	3000	(3.92)	2994
F	3125	(3.63)	3150	(3.65)	..
G	3275	(3.80)	3270	(3.82)	3275
H	3410	(3.87)	3400	(3.85)	3413
I	3580	(3.69)	3575	(3.70)	3593
I′	3655	(3.41)	...	..	3650
J	3755	(2.73)	3730	(2.70)	3745
K	3845	(3.07)	3840	(2.95)	3840

[a] See Fig. 1.

It will be observed that agreement in both wave lengths and intensities of the maxima is very satisfactory except for the intensities of the two most strongly absorbing bands C and D for which the intensity measurements of Mayneord and Roe are appreciably high.

Monomethyl and Dimethyl Derivatives of 1,2-Benzanthracene.—The spectra and intensities measured for ten of the derivatives are given in Table II. All these give curves of the same general shape. The bands A, B, C, D and H are of approximately constant intensity throughout the series. Noticeable variations occur in the bands E, J, and K, E and J are missing entirely in the 9-methyl, 5,8-dimethyl and 9,10-dimethyl derivatives. The band K is missing also in the 10-methyl compound and is ill-defined in the 9-methyl compound. Variations are also to be observed in the degree of resolution of bands I and I′. Resolution into two separate bands is well-defined in the 1′-, 4-, 5-, 8- and 10-monomethyl compounds and in the 5,8-derivative but is absent in the others. It can just be resolved in the parent hydrocarbon. It does not seem possible to asso-

TABLE II

POSITION OF THE MAXIMA AND CORRESPONDING INTENSITIES (LOG E_{molar}) IN THE ULTRAVIOLET ABSORPTION SPECTRA OF ALKYL DERIVATIVES OF 1,2-BENZANTHRACENE (SOLVENT ETHANOL)

Derivative of 1,2-benzanthracene	M. p., °C.	Absorption data											
		A	B	C	D	E	F	G	H	I	I′	J	K
1,2-Benzanthracene[a]	160.5–	2540	2665	2765	2870	2995	3125	3275	3410	3580	3655	3755	3845
	161	4.56	4.60	4.85	4.95	3.99	3.63	3.80	3.87	3.69	3.41	2.73	3.07
1′-Methyl[b]	138.5–	2540	2675	2770	2875	2995	..	3260	3410	3585	3670	(3770)	3875
	139.2	4.50	4.68	4.89	4.90	4.00	..	..	3.88	3.81	3.48	2.74	3.20
4-Methyl[c]	124.1–	2580	2670	2785	2885	3015	..	3280	3420	3585	3650	3760	3850
	124.6	4.59	4.59	4.87	4.96	3.84	..	..	3.83	3.75	3.62	2.95	3.15
5-Methyl[d]	158.5–	(2625)	2695	2785	2890	3005	(3245)	3320	3460	3610	3675	3790	3860
	159	4.60	4.68	4.82	4.94	3.90	(3.75)	3.85	3.91	3.78	3.76	2.95	3.08
8-Methyl[e]	118–	2590	2690	2795	2900	3005	3160	3310	3460	3605	3670	3770	3865
	118.5	4.57	4.64	4.84	4.96	3.90	3.67	3.84	3.88	3.66	3.60	2.94	3.06
9-Methyl[f]		2580	2690	2790	2905	..	(3220)	3360	3515	(3670)	..	..	(3930)
		4.62	4.64	4.87	4.94	..	(3.66)	3.81	3.88	3.81	..	..	3.02
10-Methyl[d]	140.2–	2575	2705	2800	2915	3025	3210	3345	3545	3650	3720	3835	3895
	140.8	4.54	4.60	4.87	4.98	4.02	3.66	3.82	3.94	3.75	3.78	3.03	3.05
5,8-Dimethyl[g]	134.4–	2620	2715	2820	2925	..	3200	3360	3520	3625	3710	..	3865
	134.7	4.62	4.67	4.84	4.93	..	3.64	3.85	3.88	3.72	3.72	..	3.10
5,10-Dimethyl[d]	147–	2650	2725	2830	2945	3050	(3280)	3400	3580	3775	..	..	3925
	147.5	4.60	4.63	4.86	4.93	3.86	3.60	3.88	3.97	3.87	..	..	3.18
8,10-Dimethyl[g]	145.5–	2610	2730	2825	2950	3045	3235	3375	3560	3735	..	3830	3915
	146.5	4.57	4.59	4.78	4.96	4.03	3.71	3.89	3.97	3.77	..	3.12	3.08
9,10-Dimethyl[h]	122.7–	2625	2735	2850	2965	..	(3300)	3450	3640	3840	..	..	3900
	123.4	4.50	4.58	4.80	4.90	..	..	3.83	3.94	3.83	..	..	..

[a] Prepared by Dr. H. J. Creech by modification of method due to Bachmann, *J. Org. Chem.*, **1**, 349 (1936). [b] Fieser and Seligman, THIS JOURNAL, **60**, 170 (1938). [c] Fieser and Jones, *ibid.*, **60**, 1940 (1938). [d] Fieser and Newman, *ibid.*, **58**, 2376 (1936). [e] Fieser and Johnson, *ibid.*, **61**, 168 (1939). [f] Newman, *ibid.*, **59**, 1003 (1937). [g] Fieser and Johnson, *ibid.*, **61**, 1647 (1939). [h] Prepared by Mr. Webber by method due to Bachmann.

ciate these variations with the structural differences between the molecules but it can be concluded that substitution at the 9- and 10-positions seems to cause more loss of resolution than substitution elsewhere.

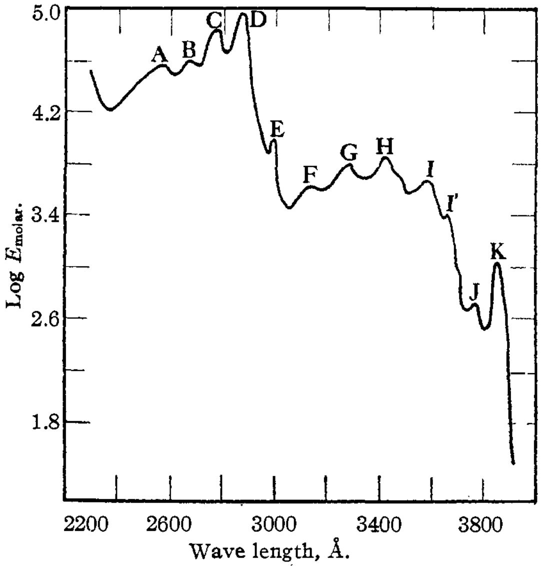


Fig. 1.—1,2-Benzanthracene.

The absorption curves of these various substances are not published since they are superficially very similar. The absorption spectrum of 1,2-benzanthracene itself is given in Fig. 1.

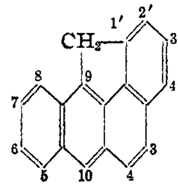
TABLE III

POSITIONS AND INTENSITIES OF THE ABSORPTION MAXIMA OF 1',9-METHYLENE-1,2-BENZANTHRACENE[a] (SOLVENT ETHANOL)

Wave length	Intensity	Wave length	Intensity
2565 Å.	(4.59)	3330	(3.89)
2720	(4.51)	3415	(3.81)
2805	(4.69)	3505	(3.93)
2890	(4.71)	3600	(3.73)
2930	(4.62)	3690	(3.87)
3060	(3.89)	(3775)[b]	(3.05)
3205	(3.64)	3870	(3.50)

[a] Fieser and Cason, THIS JOURNAL, **61**, 1740 (1939).
[b] Inflection only.

1',9-Methylene-1,2-benzanthracene. (I).—



(I)

Absorption measurements made on this compound show it to have a spectrum differing in many respects from that of the other derivatives (Fig. 2). The two bands C and D are here replaced by a system of one broad and two sharp maxima, all less intense. There is also more resolution in the longer wave region there being ten maxima resolved in the E–K range instead of eight. The act of bridge formation is not in itself sufficient cause for this change since cholanthrene and 20-methylcholanthrene show spectra of the normal type. Examination of Stuart models suggests that considerably more strain is present in the 1',9-methylene structure than in the 5,10-dimethylene bridge of cholanthrene and the changes produced in the spectrum may be associated with this condition.

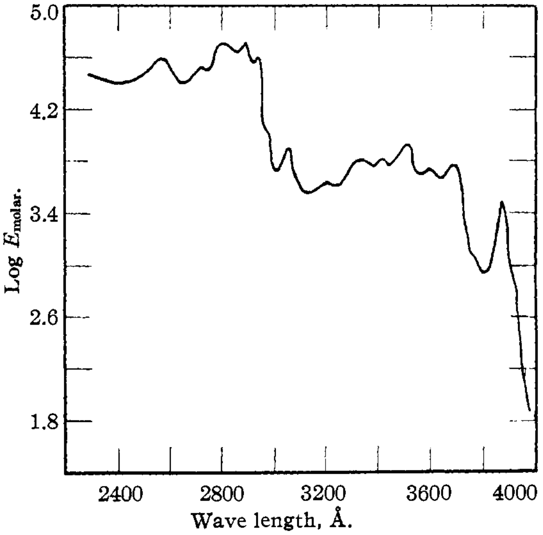


Fig. 2.—1',9-Methylene-1,2-benzanthracene.

Bathochromic Shifts Produced by Substitution.—The introduction of an alkyl group into an aromatic compound produces a shift of the absorption curve toward longer wave lengths (bathochromic shift). Klingstedt[10] found a shift of 820 cm.$^{-1}$ for toluene with respect to benzene and de Laszlo[11] observed shifts of 330 and 690 cm.$^{-1}$ for α- and β-methylnaphthalenes, respectively, in comparison with naphthalene.

An analysis of the alkyl 1,2-benzanthracenes shows that the shift produced differs very much according to the position of substitution. In making such an analysis the question arises as to what criterion should be taken in determining the relative shift. The displacement of each individual maximum may be measured (preferably on a frequency scale) and a mean value deduced but

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[10] Klingstedt, *Compt. rend.*, **175**, 1065 (1921).
[11] De Laszlo, *Z. physik. Chem.*, **118**, 369 (1925).

TABLE IV

BATHOCHROMIC SHIFT OF BAND D AND THE CARCINOGENIC ACTIVITY AS INDICATED BY THE LATENT PERIOD IN TUMOR PRODUCTION IN MICE[a]

Derivative of 1,2-benzanthracene	Max., Å.	Δ Max., Å.	Activity	
			Subcutaneous	Skin Painting
1,2-Benzanthracene	2870	0	Inactive	Inactive
1′-Methyl-	2875	5	Inactive	Inactive
7-Methyl-	2880	10	1 Tumor in 39 weeks	Inactive
6,7-Dimethyl-	2880	10	Inactive	Very slightly active
6,7-Cyclopenteno-	2880	10	......	About 43 weeks
4-Methyl-	2885	15	Active[b]	1 Papilloma
5-Methyl-	2890	20	27 Weeks	44 Weeks
6-Methyl-	2890	20	......	44/102 Weeks
6-Isopropyl-	2895	25	......	41 Weeks
8-Methyl-	2900	30	Inactive[b]	.....
9-Methyl-	2905	35	24 Weeks	.....
10-Methyl-	2915	45	14/18 Weeks	30 Weeks
10-Isopropyl-	2920	50	Inactive	Inactive
5,8-Dimethyl-	2925	55	......	.....
5,6-Cyclopenteno-	2930	60	......	26.4 Weeks
5,10-Dimethyl-	2945	75	15 Weeks	16 Weeks
8,10-Dimethyl-	2950	80	......	.....
Cholanthrene	2950	80	13.5 Weeks	15.7 Weeks
(3,4-Benzpyrene)	2955	85	15.3 Weeks	19.1 Weeks
9,10-Dimethyl-	2965	95	Active	Very active
20-Methylcholanthrene	2970	100	13 Weeks	18 Weeks

[a] Fieser, *Am. J. Cancer*, **34**, 37 (1938). [b] Shear, private communication.

such a method is open to criticism as the widths of the bands vary considerably and with them the degree of accuracy possible in determining the exact position of the maximum; furthermore, as the number of bands which can be resolved in all the compounds is not the same, such a mean would have little physical significance. Band D is the most intense and is quite narrow and obviously corresponds to some major electronic excitation of the molecule. In view of this steepness, the position of the maximum can be determined more accurately than that of the other bands and it was therefore decided to compare the position of the maximum of this band only in the various derivatives.

In Table IV, column 2 the positions of the maximum of band D of twenty derivatives of 1,2-benzanthracene are arranged in increasing order of bathochromic shift. The values of the compounds in italics are interpolated from the graphs of Mayneord and Roe.[4]

Bathochromic Shift and Carcinogenic Activity.—Many of the alkyl and ace-1,2-benzanthracenes are carcinogenically active and it is interesting to examine whether any relation can be found between the spectrum of these compounds and their physiological action. An attempt to discover such a relation implies that the carcinogenic activity can be assessed quantitatively or at least that the compounds can be arranged in order of increasing carcinogenic potency; much attention has been given to this subject in the laboratories of Fieser,[5] Shear[6] and Cook.[7] The carcinogenic activity is often expressed in terms of the latent period between the commencement of the administration and the development of tumors in mice. In the case of three compounds which have been very thoroughly investigated, *viz.*, 1,2,5,6-dibenzanthracene, 20-methylcholanthrene and 3,4-benzpyrene it has been shown that many factors enter into the determination of this latent period. These include the genetic history, age and sex of the mouse, and the dosage, manner and medium of administration of the hydrocarbon. Cook has usually administered the compound by skin painting producing a carcinoma, while Shear has largely employed subcutaneous injection to give a sarcoma of the connective tissue.

The carcinogenic activity of most of these alkyl 1,2-benzanthracenes has so far been examined only in a superficial manner; determinations of the latent period prior to tumor production have been made on only ten or twenty mice and not necessarily under comparable conditions of genetic strain, age, sex or dosage, etc. The data at present available are summarized in Table IV (Fieser[5]) and it will be observed that some correlation can be traced between the carcinogenic activity and the bathochromic shift of band D. Considering first the monomethyl derivatives, of the twelve possible isomers eight have been examined and the carcinogenically inactive 1′- and 7-methyl compounds show a very small shift (5, 10 Å.) whereas the 10-methyl compound, the most active of this group, has the largest shift (45 Å.). The 9,10-dimethyl compound, which is highly active, particularly with regard to skin painting, and cholanthrene both show large shifts (95, 80 Å.) while 20-methylcholanthrene which acts very rapidly on both subcutaneous and cutaneous tissue has the maximum shift of 100 Å. The introduction of a second alkyl group into an alkylaromatic hydrocarbon causes a further shift of the spectrum to longer wave lengths, yet in the feebly carcinogenic 6,7-dimethyl compound the shift is small (10 Å.), less than that of many of the monomethyl derivatives. The relative carcinogenic activities of the 6,7- and 5,6-cyclopenteno derivatives are also in agreement with their spectral shifts.

The correlation, however, is not without exceptions. The 10-isopropyl compound is inactive yet the bathochromic shift is quite large. Here there is a second factor introduced in the lengthening of the side chain and it is known that even the extreme lengthening of an alkyl chain may produce little change in the absorption of an attached chromophore (*cf.* the spectra of acetic and palmitic acids[12]) while its effect on the physiological properties may be profound. The 8-methyl compound is a more significant exception. It has failed to produce tumors when the crystalline substance was repeatedly injected into twenty mice over a period of ten months (Shear[13]).

3,4-Benzpyrene is included in Table IV in parentheses since although the short wave region of the spectrum is like that of 1,2-benzanthracene the longer wave part is different. The spectrum of 1,2,5,6-dibenzanthracene is quite different and cannot be included in this analysis. Of the carcinogenically active hydrocarbons not closely related to 1,2-benzanthracene, the 3,4-benzphenanthrene group is the most interesting, particularly the 2-methyl compound, which is very potent when applied to the skin[14] but apparently inactive subcutaneously.[13] The absorption spectrum of 3,4-benzphenanthrene differs considerably from that of 1,2-benzanthracene.[4]

The magnitude of these spectral shifts corresponds to relatively small differences in the absorption energy involved. The general similarity in shape and constancy of intensity among all the curves show that the presence or absence of an alkyl group can have only a minor influence on the electronic activations of the molecule associated with light absorption in this near ultraviolet region of the spectrum. On the other hand, the observed displacements are considerably greater than the experimental errors of measurement. At present the mode of action of a carcinogen is obscure and the great differences in activity among compounds of closely similar structure show that the controlling factors may be exceedingly subtle. The small spectral shifts and variations in carcinogenic activity may be independent consequences of some such common structural influence.

Acknowledgment.—The author wishes to thank Professor L. F. Fieser for his encouragement and advice during the progress of this research, the Commonwealth Fund for fellowship support and Dr. Hugh H. Darby for many valuable suggestions regarding the setting up of the apparatus. Funds for the installation of the spectrograph were derived from a grant to Professor Fieser from the National Advisory Cancer Council.

Summary

The ultraviolet absorption spectra of 1,2-benzanthracene and of ten mono and dimethyl derivatives have been examined and found to be closely similar in shape and intensity. Considerable variation is observed in the bathochromic shift of the position of the maximum of the most intense band and this appears to show some correlation with the variation in the carcinogenic activity of the hydrocarbons.

The spectrum of 1′,9-methylene-1,2-benzanthracene differs markedly from that of the other derivatives and this is considered possibly to be due to steric strain in the molecule.

The spectrographic equipment recently installed in these laboratories is also described.

CAMBRIDGE, MASS. RECEIVED JUNE 14, 1939

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(12) Ley and Arends, *Z. physik. Chem.*, **B17**, 183 (1935).

(13) Private communication.

(14) Bachmann, Cook, Dansi, deWorms, Haslewood, Hewett and Robinson, *Proc. Roy. Soc.* (London), **B123**, 343 (1937).