If the volume of the former solution is V' and that of the latter is V'', it is evident that

$$N'_B = f'_B N_A/V', \quad N''_B = f''_B N_A/V'', \quad N'_P + N'_e =$$
$$f'_t N_A/V', \quad N''_P + N''_e = f''_t N_A/V'' \quad (7)$$

where f'_t and f'_B denote, respectively, the molar fraction of trans-1,4-dichlorocyclohexane and that of benzene in the former solution, f''_t and f''_B have, respectively, the same meaning concerning the latter, and N_A is the Avogadro number. By combining equations (6) and (7), we may write

$$X'_P/X''_P = I'_P f'_B f''_t/I''_P f''_B f'_t \quad (8)$$

where X'_P and X''_P are given by the relations (9)

$$X'_P = N'_P/(N'_e + N'_P), \quad X''_P = N''_P/(N''_e + N''_P) \quad (9)$$

Similarly, we may write

$$X'_e/X''_e = I'_e f'_B f''_t/I''_e f''_B f'_t \quad (10)$$

where X'_e and X''_e denote the similar fractions as represented in equation (9), and it is evident that

$$X_e + X'_P = X''_e + X''_P = 1 \quad (11)$$

From equations (8), (10) and (11) we can calculate the values for X'_e, X'_P, X''_e and X''_P. The values for X'_P and X''_P thus obtained are, respectively, 0.58 and 0.66. Therefore, by using equation (1) the value for S_e/S_p is estimated to be 2.0.

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Spectra of Azlactones. I. Azlactones Derived from Substituted Benzaldehydes and Hippuric and Nitrohippuric Acids

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The absorption spectra of a series of azlactones obtained by condensation of hippuric acid, o-, m- and p-nitrohippuric acids, with benzaldehyde and substituted benzaldehydes, have been determined in acetic acid solution up to 255 mμ. All the azlactones show a band of high intensity, each with a maximum varying with substitution, at 346–430 mμ. In some azlactones, a second, less intense band, with a maximum at 256–310 mμ is found. It is absent in azlactones where a nitro group is placed ortho or meta, in phenyls R_1 or R_2 (Formula I). Some correlations, between the position of the first maximum in the absorption spectra and the substituents, are described.

The azlactones, obtained by condensation of aromatic aldehydes with hippuric acid by the Plöchl–Erlenmeyer reaction, contain a conjugate system of two double bonds with two end phenyl nuclei, R_1 and R_2 (I). The fact that the azlactones can be easily prepared and that a wide variation of substitution in one or both phenyls is a possibility, makes this class of compounds particularly favorable for the study of the influence of substituents on the absorption spectra.

The first reports on the absorption spectra of the azlactones are those of Asahina[1] whose data are very difficult to interpret because in many cases the data are given only graphically. Recently, Carter and Hinman[2] reported the ultraviolet absorption spectrum of one azlactone, the 2-phenyl-4-p-methoxybenzal-5-oxazolone (No. 13), while Bennett and Niemann[3] reported the absorption spectra in the ultraviolet and the visible of 2-phenyl-4-p-fluorobenzal oxazolone and of 2-phenyl-4-m-fluorobenzal oxazolone. Both Asahina and Carter found a band with a maximum at about 250–260 mμ. At longer wave lengths Bennett and Niemann found a stronger band with a maximum at about 360–390 mμ. More recently Schueler and Wang[4] determined the absorption spectra of 28 azlactones and except for a few cases, found two maxima, at shorter wave lengths than other workers, one at about 220–232 mμ, the other at 284–323 mμ.

The authors have determined the absorption spectra for 71 azlactones in acetic acid solution (Table I, Part A) and for 5 of the above mentioned azlactones in absolute ethanol (Table I, Part B).

Unfortunately, owing to the instability of the azlactones derived from the nitrohippuric acids, in dilute ethanol solutions and to their insolubility in other less absorbing solvents, the authors determined the spectra of the azlactones studied in acetic acid solution, limiting the observations up to 255 mμ. The spectra of some of the azlactones derived from hippuric acid, in ethanol (No. 1, 13, 24, 28 and 48), showed in each case that the maxima were not displaced by changing the solvent. Slight variations in the value of ε were observed.

The spectrum of all azlactones showed an intense absorption band, with a maximum at about 361–430 mμ, varying with substitution. In some cases a second less intense band, with a maximum at 256–310 mμ was found. This same band was definitely absent, in azlactones where a nitro group is placed in ortho or meta position, in one or both phenyls R_1 and R_2.

The authors' experimental data for 12 of the above mentioned 71 azlactones does not agree with that of Schueler and Wang.[4] In each case the maximum is always displaced toward the longer wave lengths and are located in the same region as reported by Carter and Hinman[2] and by Bennett and Niemann.[3]

In the case of the particular azlactone studied by Carter and Hinman[2] the authors were able to check their data (see Table I, Part B, No. 13).

For most of the azlactones studied by Schueler and Wang[4] and the authors, the latter found a positive difference of about 74–77 mμ between their data and that reported by Schueler and Wang[4] for the maximum present at longer wave lengths, and

(1) T. Asahina, Bull. Chem. Soc. Japan, 4, 202 (1929); 5, 354 (1930).

(2) H. M. Carter and J. W. Hinman, J. Biol. Chem., 178, 403 (1949).

(3) E. L. Bennett and C. Niemann, THIS JOURNAL, 72, 1803 (1950).

(4) F. W. Schueler and S. C. Wang, ibid., 72, 2220 (1950); Schueler and C. Hanna, ibid., 73, 3528 (1951).

TABLE I

SPECTRA OF AZLACTONES OF TYPE R₁—CH=C——N
$$R_1-CH=C\overset{\displaystyle \underset{\underset{O}{\diagdown\diagup}}{\overset{|}{CO}}\ \ \overset{\displaystyle N}{\underset{C-R_2}{||}}}{}$$

I

No.	R₁ (Azlactones)	R₂	Max. I mμ	ε × 10⁻³	Max. II mμ	ε × 10⁻³

Part A. In acetic acid

No.	R₁	R₂	Max. I $m\mu$	$\epsilon \times 10^{-3}$	Max. II $m\mu$	$\epsilon \times 10^{-3}$
1	C_6H_5-	C_6H_5-	361[a]	37.6	259	15.6
2	C_6H_5-	$o\text{-}NO_2C_6H_4-$	365	26.6	...	..
3	C_6H_5-	$m\text{-}NO_2C_6H_4-$	364	33.2	...	..
4	C_6H_5-	$p\text{-}NO_2C_6H_4-$	381	33.0	279	9.0
5	$o\text{-}CH_3OC_6H_4-$	C_6H_5-	386	31.0	256	13.6
6	$o\text{-}CH_3OC_6H_4-$	$o\text{-}NO_2C_6H_4-$	396	23.6	...	..
7	$o\text{-}CH_3OC_6H_4-$	$m\text{-}NO_2C_6H_4-$	393	26.6	...	..
8	$o\text{-}CH_3OC_6H_4-$	$p\text{-}NO_2C_6H_4-$	409	28.0	283	8.5
9	$m\text{-}CH_3OC_6H_4-$	C_6H_5-	366[b]	29.5	259	14.9
10	$m\text{-}CH_3OC_6H_4-$	$o\text{-}NO_2C_6H_4-$	373	22.0	...	..
11	$m\text{-}CH_3OC_6H_4-$	$m\text{-}NO_2C_6H_4-$	366	29.0	...	..
12	$m\text{-}CH_3OC_6H_4-$	$p\text{-}NO_2C_6H_4-$	387	25.3	284[c]	13.6
13	$p\text{-}CH_3OC_6H_4-$	C_6H_5-	383	39.2	259	16.4
14	$p\text{-}CH_3OC_6H_4-$	$o\text{-}NO_2C_6H_4-$	394	32.4	...	..
15	$p\text{-}CH_3OC_6H_4-$	$m\text{-}NO_2C_6H_4-$	392	40.4	...	..
16	$p\text{-}CH_3OC_6H_4-$	$p\text{-}NO_2C_6H_4-$	411	33.8	297	13.0
17	$m\text{-}CH_3COOC_6H_4-$	C_6H_5-	361[d]	37.0	260	15.5
18	$m\text{-}CH_3COOC_6H_4-$	$m\text{-}NO_2C_6H_4-$	363	31.6	...	..
19	$m\text{-}CH_3COOC_6H_4-$	$p\text{-}NO_2C_6H_4-$	379	29.8	279	12.2
20	$p\text{-}CH_3COOC_6H_4-$	C_6H_5-	365[e]	38.2	261	15.6
21	$p\text{-}CH_3COOC_6H_4-$	$o\text{-}NO_2C_6H_4-$	368	28.0	...	..
22	$p\text{-}CH_3COOC_6H_4-$	$m\text{-}NO_2C_6H_4-$	368	33.4	...	..
23	$p\text{-}CH_3COOC_6H_4-$	$p\text{-}NO_2C_6H_4-$	385	32.6	282	14.0
24	$2,3\text{-}(CH_3O)_2C_6H_3-$	C_6H_5-	367[f]	36.3	259	13.1
25	$2,3\text{-}(CH_3O)_2C_6H_3-$	$o\text{-}NO_2C_6H_4-$	371	26.2	...	..
26	$2,3\text{-}(CH_3O)_2C_6H_5$	$m\text{-}NO_2C_6H_4-$	371	31.0	...	..
27	$2,3\text{-}(CH_3O)_2C_6H_3-$	$p\text{-}NO_2C_6H_4-$	388	30.6	285	10.8
28	$3,4\text{-}(CH_3O)_2C_6H_3-$	C_6H_5-	396	34.3	264	17.9
29	$3,4\text{-}(CH_3O)_2C_6H_3-$	$o\text{-}NO_2C_6H_4-$	414	30.2	...	..
30	$3,4\text{-}(CH_3O)_2C_6H_3-$	$m\text{-}NO_2C_6H_4-$	408	33.0	...	..
31	$3,4\text{-}(CH_3O)_2C_6H_3-$	$p\text{-}NO_2C_6H_4-$	426	33.8	308	13.0
32	$3\text{-}C_2H_5O\text{-}4\text{-}CH_3OC_6H_3-$	C_6H_5-	399	34.2	264	16.6
33	$3\text{-}C_2H_5O\text{-}4\text{-}CH_3OC_6H_3-$	$o\text{-}NO_2C_6H_4-$	415	29.0	...	..
34	$3\text{-}C_2H_5O\text{-}4\text{-}CH_3OC_6H_3-$	$m\text{-}NO_2C_6H_4-$	412	31.5	...	..
35	$3\text{-}C_2H_5O\text{-}4\text{-}CH_3OC_6H_3-$	$p\text{-}NO_2C_6H_4-$	428	29.6	309	11.8
36	$4\text{-}C_2H_5O\text{-}3\text{-}CH_3OC_6H_3-$	C_6H_5-	399	35.2	264	17.2
37	$4\text{-}C_2H_5O\text{-}3\text{-}CH_3OC_6H_3-$	$o\text{-}NO_2C_6H_4-$	415	29.6	...	..
38	$4\text{-}C_2H_6O\text{-}3\text{-}CH_3OC_6H_3-$	$m\text{-}NO_2C_6H_4-$	412	32.7	...	..
39	$4\text{-}C_2H_5O\text{-}3\text{-}CH_3OC_6H_3-$	$p\text{-}NO_2C_6H_4-$	430	30.0	309	11.3
40	$3,4\text{-}(C_2H_5O)_2C_6H_3-$	C_6H_5-	401	31.4	265	17.8
41	$3,4\text{-}(C_2H_5O)_2C_6H_3-$	$o\text{-}NO_2C_6H_4-$	417	29.2	...	..
42	$3,4\text{-}(C_2H_5O)_2C_6H_3-$	$m\text{-}NO_2C_6H_4-$	414	32.0	...	..
43	$3,4\text{-}(C_2H_5O)_2C_6H_3-$	$p\text{-}NO_2C_6H_4-$	432	29.8	309	12.3
44	$3,4\text{-}CH_2O_2C_6H_3-$	C_6H_5-	394	33.4	264	18.8
45	$3,4\text{-}CH_2O_2C_6H_3-$	$o\text{-}NO_2C_6H_4-$	405	28.2	...	..
46	$3,4\text{-}CH_2O_2C_6H_3-$	$m\text{-}NO_2C_6H_4-$	404	32.8	...	..
47	$3,4\text{-}CH_2O_2C_6H_3-$	$p\text{-}NO_2C_6H_4-$	421	29.4	308	11.8
48	$3,4,5\text{-}(CH_3O)_3C_6H_2-$	C_6H_5-	385	28.2	286	8.8
49	$3,4,5\text{-}(CH_3O)_3C_6H_2-$	$o\text{-}NO_2C_6H_4-$	400	25.7	...	..
50	$3,4,5\text{-}(CH_3O)_3C_6H_2-$	$m\text{-}NO_2C_6H_4-$	397	28.8	...	..
51	$3,4,5\text{-}(CH_3O)_3C_6H_2-$	$p\text{-}NO_2C_6H_4-$	413	28.0	310	14.2
52	$4\text{-}CH_3COO\text{-}3\text{-}CH_3OC_6H_3-$	C_6H_4-	372[g]	34.8	259	16.0
53	$4\text{-}CH_3COO\text{-}3\text{-}CH_3OC_6H_3-$	$o\text{-}NO_2C_6H_4-$	382	27.0	...	..
54	$4\text{-}CH_3COO\text{-}3\text{-}CH_3OC_6H_3-$	$m\text{-}NO_2C_6H_4-$	378	29.4	...	..
55	$4\text{-}CH_3COO\text{-}3\text{-}CH_2OC_6H_3-$	$p\text{-}NO_2C_6H_4-$	395	28.6	287	13.2
56	$3\text{-}CH_3COO\text{-}4\text{-}CH_3OC_6H_3-$	C_6H_5-	380[h]	39.4	259	17.2
57	$3\text{-}CH_3COO\text{-}4\text{-}CH_3OC_6H_3-$	$o\text{-}NO_2C_6H_4-$	391	30.0	...	..
58	$3\text{-}CH_3COO\text{-}4\text{-}CH_3OC_6H_3-$	$m\text{-}NO_2C_6H_4-$	388	34.6	...	..

TABLE I (Continued)

No.	R₁ (Azlactones)	R₂	Max. I mμ	Max. I $\epsilon \times 10^{-3}$	Max. II mμ	Max. II $\epsilon \times 10^{-3}$
59	3-CH₃COO-4-CH₃OC₆H₃-	p-NO₂C₆H₄-	407	33.8	296	12.4
60	o-NO₂C₆H₄-	C₆H₅-	360	24.2	...	..
61	o-NO₂C₆H₄-	o-NO₂C₆H₄-	353	19.0	...	..
62	o-NO₂C₆H₄-	m-NO₂C₆H₄-	355	22.0	...	..
63	o-NO₂C₆H₄-	p-NO₂C₆H₄-	364	24.4	261	14.5
64	m-NO₂C₆H₄-	C₆H₅-	359ⁱ	33.3	...	..
65	m-NO₂C₆H₄-	o-NO₂C₆H₄-	346ʲ	24.5	...	..
66	m-NO₂C₆H₄-	m-NO₂C₆H₄-	359ᵏ	27.6	...	..
67	m-NO₂C₆H₄-	p-NO₂C₆H₄-	361	29.6	271	16.0
68	p-NO₂C₆H₄-	C₆H₅-	376	36.6	271	11.8
69	p-NO₂C₆H₄-	o-NO₂C₆H₄-	373	29.8	...	..
70	p-NO₂C₆H₄-	m-NO₂C₆H₄-	373	34.8	...	..
71	p-NO₂C₆H₄-	p-NO₂C₆H₄-	383	36.6	278	9.8

Part B. In absolute ethanol[l]

No.	R₁ (Azlactones)	R₂	Max. I mμ	Max. I $\epsilon \times 10^{-3}$	Max. II mμ	Max. II $\epsilon \times 10^{-3}$
1	C₆H₅-	C₆H₅-	360ᵐ	38.7	259	15.0
15	p-CH₃OC₆H₄	C₆H₅-	383	40.0	259ⁿ	17.3
24	2,3-(CH₃O)₂C₆H₃-	C₆H₅-	367ᵒ	37.2	259	12.6
28	3,4-(CH₃O)₂C₆H₃-	C₆H₅-	398	32.4	264	16.4
48	3,4,5-(CH₃O)₃C₆H₂-	C₆H₅-	385	26.0	286ᵖ	7.5

ᵃ A.M. (another maximum) at 378 mμ; $\epsilon \times 10^{-3}$ 27.5. ᵇ A.M. at 383 mμ; $\epsilon \times 10^{-3}$ 24.3. ᶜ A.M. at 270 mμ; $\epsilon \times 10^{-3}$ 13.6. ᵈ A.M. at 378 mμ; $\epsilon \times 10^{-3}$ 27.3. ᵉ A.M. at 382 mμ; $\epsilon \times 10^{-3}$ 28.6. ᶠ A.M. at 384 mμ; $\epsilon \times 10^{-3}$ 27.3. ᵍ A.M. at 382 mμ; $\epsilon \times 10^{-3}$ 28.6. ʰ A.M. at 394 mμ; $\epsilon \times 10^{-3}$ 34.4. ⁱ A.M. at 378 mμ; $\epsilon \times 10^{-3}$ 22.6. ʲ A.M. at 358 mμ; $\epsilon \times 10^{-3}$ 24.1. ᵏ A.M. at 344 mμ; $\epsilon \times 10^{-3}$ 25.5. ˡ Azlactones are numbered the same as in Part A. ᵐ A.M. at 379 mμ; $\epsilon \times 10^{-3}$ 29.2; 246 mμ; $\epsilon \times 10^{-3}$ 14.1; 240 mμ; $\epsilon \times 10^{-3}$ 13.0. ⁿA.M. at 252 mμ; $\epsilon \times 10^{-3}$ 16.0. For this azlactone Carter and Hinman[2] give the following maxima in the ultraviolet: 251 mμ; $\epsilon \times 10^{-3}$ 16.0; 259.5 mμ; $\epsilon \times 10^{-3}$ 17.0, and a shoulder at 280 mμ. ᵒ A.M. at 386 mμ; $\epsilon \times 10^{-3}$ 37.2. ᵖ A.M. at 254 mμ; $\epsilon \times 10^{-3}$ 11.4.

a positive difference of 24–30 mμ for the maximum located at shorter wave lengths.[5]

The origin of the absorption spectrum of the azlactones is discussed by Schueler and Wang.[4] They pointed out that two different conjugated systems are present in these compounds
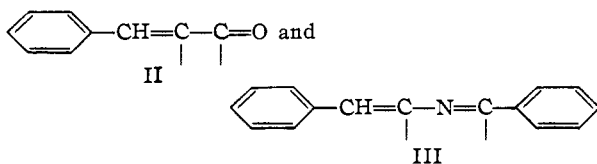
and suggested that the chromophore responsible for the spectrum is most likely system (II).

The authors do not agree with this interpretation by Schueler and Wang[4] which was reasoned from a comparison of their data with the spectra of α,β-unsaturated ketones.[6]

Since the authors found experimentally that the maxima of the azlactones are displaced to longer wave lengths than those reported by Schueler and Wang[4] and since they therefore no longer agree with the maxima for the α,β-unsaturated ketones, the principal argument for attributing an important part in determining the absorption spectra of the azlactones to the conjugated system II is invalid.

On the other hand, the spectra of diphenylbutadiene (λmax 324 mμ), dibenzalazine (λmax 300 mμ)[7] and cinnamalaniline (λmax 300 mμ),[8] with a conjugate system similar to that present in the azlactones

(III) each have a maximum at a wave length nearer to the maximum of the comparable azlactone (No. 1), than to the related α,β-unsaturated ketones.

In the opinion of the authors the conjugated system (III) is responsible for the first absorption band of the azlactones. The fact that the first maximum in the azlactones is displaced to longer wave lengths than in the simpler compounds mentioned can be explained by the replacement of carbon by a nitrogen atom in the butadiene system[9] or to cross conjugation with the keto group present in the oxazolone ring.[10]

It is possible that this band with a maxima between 361 and 430 mμ according to the substituent is superimposed on another less intense band, because in some azlactones, another maximum of less intensity is found at longer wave lengths (No, 1, 9, 17, 20, 24, 32, 56, 65 and 66).

The second, less intense band, found in some azlactones with a maxima between 256 and 310 mμ appears to be produced by partial chromophores in the sense of Lewis and Calvin.[11]

Partial chromophores in the azlactones are, for instance, the unsaturated ketone structure (II) and structures such as

The authors believe that chromophores (IV) and (V) are responsible for the second maxima. The

(5) The authors checked their spectrophotometer as described in the Experimental Part and their figures are correct to the accuracy of the apparatus.

(6) A. L. Wilds, L. W. Beck, W. J. Close, C. Djerassi, J. A. Johnson, T. L. Johnson and C. H. Shunk, THIS JOURNAL, 69, 1985 (1947).

(7) R. D. Radulescu and V. Alexa, Ber., 64, 2230 (1931).

(8) L. Ferguson and G. E. K. Branch, THIS JOURNAL, 66, 1467 (1944).

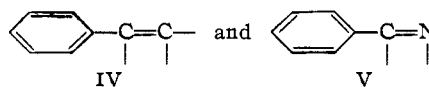(9) L. K. Evans and A. E. Gillam, J. Chem. Soc., 565 (1943), have found that in simple aliphatic compounds, the system C=C—C=N absorbs at longer wave lengths, than the system C=C—C=C.

(10) A. Radulescu, Ber., 64, 2243 (1931), found that dibenzalacetone with a keto group, conjugated with two carbon-to-carbon double bonds, has a λmax 330 mμ.

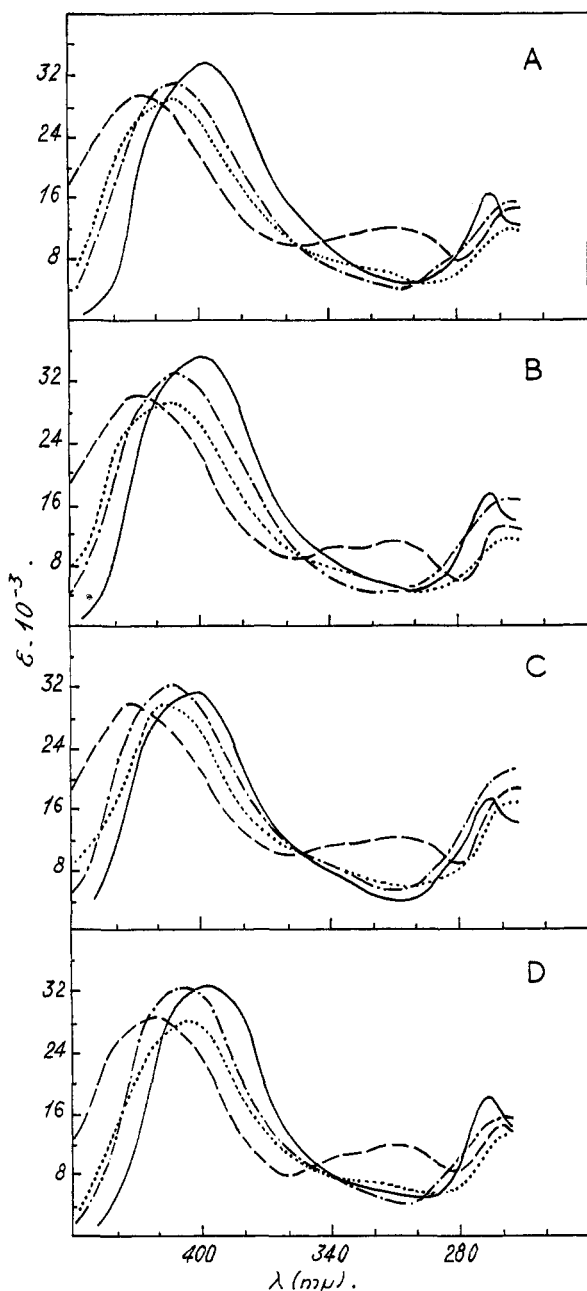(11) G. N. Lewis and M. Calvin, Chem. Revs., 25, 311 (1939).

Fig. 1.—Azlactones (I) No. 1–16: A, R_1 = C_6H_5-; B, R_1 = o-CH₃OC₆H₄-; C, R_1 = m-CH₃OC₆H₄-; D, R_1 = CH₃OC₆H₄-, R_2 = C₆H₅-, ———; R_2 = o-NO₂C₆H₄-, ⋯⋯⋯; R_2 = m-NO₂C₆H₄, ———; R_2 = p-NO₂C₆H₄, — - — - —.

Fig. 2.—Azlactones (I) No. 17–31: A, R_1 = m-CH₃-COOC₆H₄-; B, R_1 = p-CH₃COOC₆H₄-; C, R_1 = 2,3-(CH₃O)₂C₆H₃-; D, R_1 = 3,4-(CH₃O)₂C₆H₃-, R_2 = C₆H₅-, ———; R_2 = o-NO₂C₆H₄-, ⋯⋯⋯; R_2 = m-NO₂-C₆H₄, ———; R_2 = p-NO₂C₆H₄-, — - — - —.

α,β-unsaturated ketone structure (II) can be eliminated because the spectra of such ketones[6] exhibit maxima that are about 30 mμ from the second maxima of the corresponding azlactones. Whereas the absorption spectra of styrene[12] (structure IV) exhibit a maximum at 244 mμ and Grammaticakis[13] reports that oxime and imines derived from substituted benzaldehydes (structure V) exhibit maxima at 250–275 mμ, giving a difference from the second maximum of the corresponding azlactones of about 10 mμ.

This second band is also found in the spectra of some compounds, with a conjugated system of two double bonds, with two end phenyls, as in cinnamalaniline.[8]

Influence of Substitution in Phenyl R_1.—If the unsubstituted azlactone (No. 1) is used as a reference compound, it can be seen from the data in Table I that the introduction of one CH₃O–, p-NO₂– or p-CH₃COO– group into phenyl R_1 produces a bathochromic shift in the first maximum, whereas a m-CH₃COO– group gives no change, and a m-NO₂– or an o-NO₂– gives hypsochromic shifts. The order of

(12) M. Pestemer, T. Langer and F. Manchen, *Monatsh.*, **68**, 326 (1936).

(13) P. Grammaticakis, *Bull. soc. chim. France*, **8**, 427 (1941).

Fig. 3.—Azlactones (I) No. 32–47: A, R₁ = 3-C₂H₅O-4-CH₃OC₆H₃-; B, R₂ = 4-C₂H₅O-3-CH₃OC₆H₃-; C, R₁ = 3,4-(C₂H₅O)₂C₆H₃-; D, R₁ = 3,4-CH₂O₂C₆H₃-, R₂ = C₆H₅-, ——; R₂ = o-NO₂C₆H₄-, ...; R₂ = m-NO₂-C₆H₄-, -------; R₂ = p-NO₂C₆H₄-, - - - - -.

Fig. 4.—Azlactones (I) No. 48–59: A, R₁ = 3,4,5-(CH₃O)₃-C₆H₂-; B, R₁ = 4-CH₃COO-3-CH₃OC₆H₃-; C, R₁ = 3-CH₃-COO-4-CH₃OC₆H₃-; R₂ = C₆H₅-, ——; R₂ = o-NO₂C₆H₄-, ...; R₂ = m-NO₂C₆H₄-, --------; R₂ = p-NO₂C₆H₄-, - - - - -.

activities as measured by the value of the displacement of the maximum is o-CH₃O- > p-CH₃O- > p-NO₂- > m-CH₃O- > p-CH₃COO- > H = m-CH₃COO- > m-NO₂- > o-NO₂-.

Whilst it is difficult to discuss in detail the reasons for the activity of each group, it can be seen that groups with a high mesomeric effect (CH₃O-, NO₂-) when placed at positions ortho or para, where this effect can work through the conjugated system of the azlactone, should have the highest activity. The o-NO₂- is an exception because a hypsochromic shift is produced. This must be the result of the ortho effect, which has been described in

the absorption spectra of aromatic compounds, with an o-NO₂- group.[14]

This effect is attributed to steric influences and especially its capacity of decreasing the possibility of coplanarity in the molecules. Another result of this influence is the decreasing intensity of the absorption observed.

Groups with a low mesomeric effect, even when placed at the proper positions (p-CH₃COO-), do not have a high activity. When the mesomeric effect cannot operate, the activity is low (m-CH₃O-, m-CH₃COO-) or even hypsochromic shifts are observed (m-NO₂-).

A second maximum, at lower wave lengths and of less intensity, usually follows the displacement of the first maximum. It is absent when an o-NO₂- or m-NO₂- group is present in phenyl R₁.

Similarity in the spectra of ortho and meta substituted compounds have been observed in some cases[15] but the reasons for the absence of the second

(14) B. Williamson and W. H. Rodebush, THIS JOURNAL, 63, 3018 (1941); W. R. Remington, ibid., 67, 1838 (1945); W. G. Brown and G. Reagen, ibid., 69, 1032 (1947).

(15) L. Doub and J. M. Vandenbelt, ibid., 71, 2414 (1949); C. M. Moser and A. I. Kohlenberg, J. Chem. Soc., 804 (1951).

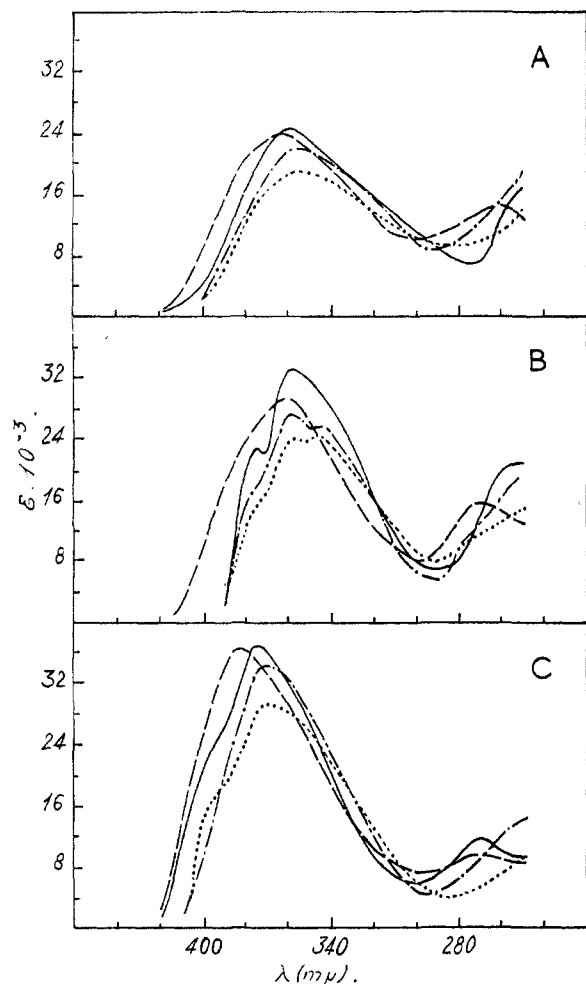Fig. 5.—Azlactones (I) No. 60–71: A, R_1 = o-NO$_2$C$_6$H$_4$-;
B, R_1 = m-NO$_2$C$_6$H$_4$-; C, R_1 = p-NO$_2$C$_6$H$_4$-; R_2 = C$_6$H$_5$-,
——; R_2 = o-NO$_2$C$_6$H$_4$-, ...; R_2 = m-NO$_2$C$_6$H$_4$-,
---------; R_2 = p-NO$_2$C$_6$H$_4$-, - - - - - - - -.

maximum are difficult to state, especially because, owing to the experimental conditions, the spectra could be observed only at 255 mμ.

When two or more substituents of the type indicated above are introduced into phenyl R_1 with one of them in the meta, and the other in either the ortho or para position, a bathochromic shift is always observed; however the intensity of the shift is different if we have an ortho–meta combination or a meta–para combination. In simultaneous ortho and meta substitution, the shift is a low value and comparable to that produced by a meta substitution alone (compare No. 24–27 with No. 5–12). The effect of the weaker group predominates.

When substitution is meta and para, the shift is of almost the same value or higher than with the para substituent alone, and consequently the influence of the meta substituent in depressing the activity of the para group is very low or non-existent (compare No. 28–31 and 44–47 with 9–16; No. 52–55 with 9–12 and 20–23 and 56–59 with 13–16 and 17–19).

When three CH$_3$O- groups are present in R_1, two in meta and one in para, the shift is of the

same order as that produced by a para substitution alone (compare No. 48–51 with 13–17).

The substitution of an C$_2$H$_5$O- group for a CH$_3$O-group intensifies the bathochromic shift. This may be the result of the higher inductive effect of the ethyl group and of the higher mesomeric effect of the ethoxyl (compare No. 32–43 with 28–31).

Influence of Substitution in Phenyl R_2.—The only substituent studied was the NO$_2$- group. The activity of this group is greater when substituted in R_2 than in R_1. When either an o-NO$_2$- or a m-NO$_2$-group is substituted in R_1, it produces a hypsochromic shift, whereas when the same group is placed in a similar position in R_2, a bathochromic shift is produced (compare No. 60 and 64 with 2 and 3.) The p-NO$_2$- produces a bathochromic shift when placed in R_1 or R_2, but the value of the shift, in relation to the unsubstituted azlactone, is greater when placed in R_2 than in R_1.

It is difficult to give an explanation for this difference in activities; it may be due to the remaining part of the azlactone molecule. Take for example the case of substitution by a p-NO$_2$-group, it means that although structures (VI) and (VII) are very similar, and that the same is true for structures (VII) and (VIIa), (both of which should make a large contribution in the first excited state of the azlactones) the difference in energies must be higher for the transition VI → VIa than for VII → VIIa, and consequently compound VI must absorb at shorter wave lengths than compound VII. When a NO$_2$- is placed in ortho or para position in R_2 the second maximum is absent, the same as in the case of phenyl R_1.

VI

IVa

VII

VIIa
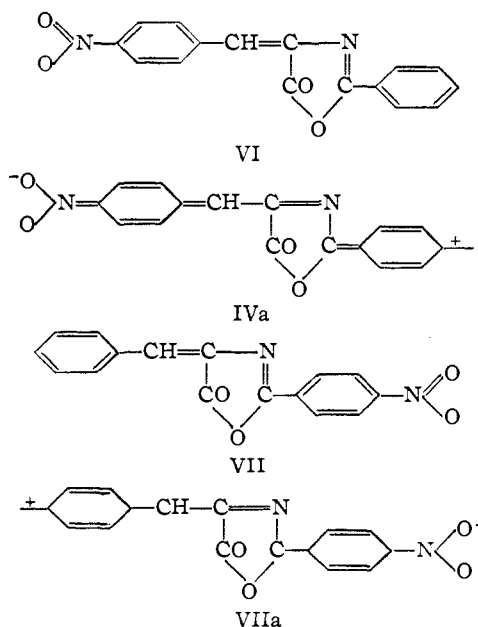
Influence of Simultaneous Substitution in Phenyls R_1 and R_2.—This influence was studied with an o-, m- or p-NO$_2$- present in R_2, and the indicated series of substituents varied in R_1.

When an o-NO$_2$- group is present in phenyl R_2, the order of activity for the different substituents placed in R_1 is the same as when R_2 is unsubstituted, even though in some cases the differ-

TABLE II

PROPERTIES AND ANALYTICAL DATA OF AZLACTONES (I)

No.[a]	R₁	R₂	Yield, %	M.p., °C	Formula	Nitrogen, % Calcd.	Found
2	C_6H_5-	$o\text{-}NO_2C_6H_4-$	43[b,f]	148	$C_{16}H_{10}N_2O_4$	9.52	9.81
3	C_6H_5-	$m\text{-}NO_2C_6H_4-$	80[b,e]	218	$C_{16}H_{10}N_2O_4$	9.52	9.90
4	C_6H_5-	$p\text{-}NO_2C_6H_4-$	62[b,f]	229	$C_{16}H_{10}N_2O_4$	9.52	9.82
6	$o\text{-}CH_3OC_6H_4-$	$o\text{-}NO_2C_6H_4-$	38[b,h]	191	$C_{17}H_{12}N_2O_5$	8.65	8.61
7	$o\text{-}CH_3OC_6H_4-$	$m\text{-}NO_2C_6H_4-$	72[e,f]	232	$C_{17}H_{12}N_2O_5$	8.65	8.65
8	$o\text{-}CH_3OC_6H_4-$	$p\text{-}NO_2C_6H_4-$	87[b,h]	248	$C_{17}H_{12}N_2O_5$	8.65	8.69
10	$m\text{-}CH_3OC_6H_4-$	$o\text{-}NO_2C_6H_4-$	53[d,f]	184	$C_{17}H_{12}N_2O_5$	8.65	8.01
11	$m\text{-}CH_3OC_6H_4$	$m\text{-}NO_2C_6H_4-$	78[e,f]	194	$C_{17}H_{12}N_2O_5$	8.65	8.97
12	$m\text{-}CH_3OC_6H_4-$	$p\text{-}NO_2C_6H_4-$	87[e,h]	226	$C_{17}H_{12}N_2O_5$	8.65	8.98
14	$p\text{-}CH_3OC_6H_4-$	$o\text{-}NO_2C_6H_4-$	38[b,h]	179	$C_{17}H_{12}N_2O_5$	8.65	8.47
15	$p\text{-}CH_3OC_6H_4-$	$m\text{-}NO_2C_6H_4-$	72[d,f]	214	$C_{17}H_{12}N_2O_5$	8.65	8.69
16	$p\text{-}CH_3OC_6H_4-$	$p\text{-}NO_2C_6H_4-$	86[b,h]	250	$C_{17}H_{12}N_2O_5$	8.65	8.55
18	$m\text{-}CH_3COOC_6H_4-$	$m\text{-}NO_2C_6H_4-$	50[e,f]	175	$C_{18}H_{12}N_2O_6$	7.95	8.11
19	$m\text{-}CH_3COOC_6H_4$	$p\text{-}NO_2C_6H_4-$	75[b,f]	181	$C_{18}H_{12}N_2O_6$	7.95	7.98
21	$p\text{-}CH_3COOC_6H_4-$	$o\text{-}NO_2C_6H_4-$	36[b,f]	178	$C_{18}H_{12}N_2O_6$	7.95	8.05
22	$p\text{-}CH_3COOC_6H_4-$	$m\text{-}NO_2C_6H_4-$	70[e,f]	201	$C_{18}H_{12}N_2O_6$	7.95	8.20
23	$p\text{-}CH_3COOC_6H_4-$	$p\text{-}NO_2C_6H_4-$	84[e,h]	236	$C_{18}H_{12}N_2O_6$	7.95	8.05
25	$2,3\text{-}(CH_3O)_2C_6H_3-$	$o\text{-}NO_2C_6H_4-$	19[b,f]	145	$C_{18}H_{14}N_2O_6$	7.91	8.22
26	$2,3\text{-}(CH_3O)_2C_6H_3-$	$m\text{-}NO_2C_6H_4-$	68[e,f]	195	$C_{18}H_{14}N_2O_6$	7.91	7.65
27	$2,3\text{-}(CH_3O)_2C_6H_3-$	$p\text{-}NO_2C_6H_4-$	72[d,f]	214	$C_{18}H_{14}N_2O_6$	7.91	8.15
29	$3,4\text{-}(CH_3O)_2C_6H_3-$	$o\text{-}NO_2C_6H_4-$	34[e,h]	177	$C_{18}H_{14}N_2O_6$	7.91	8.26
30	$3,4\text{-}(CH_3O)_2C_6H_3-$	$m\text{-}NO_2C_6H_4-$	63[b,f]	191	$C_{18}H_{14}N_2O_6$	7.91	8.17
31	$3,4\text{-}(CH_3O)_2C_6H_3-$	$p\text{-}NO_2C_6H_4-$	63[b,i]	267	$C_{18}H_{14}N_2O_6$	7.91	8.20
33	$3\text{-}C_2H_5O\text{-}4\text{-}CH_3OC_6H_3-$	$o\text{-}NO_2C_6H_4-$	41[e,h]	197	$C_{19}H_{16}N_2O_6$	7.61	7.81
34	$3\text{-}C_2H_5O\text{-}4\text{-}CH_3OC_6H_3-$	$m\text{-}NO_2C_6H_4-$	72[b,h]	199	$C_{19}H_{16}N_2O_6$	7.61	7.94
35	$3\text{-}C_2H_5O\text{-}4\text{-}CH_3OC_6H_3-$	$p\text{-}NO_2C_6H_4-$	67[b,h]	220	$C_{19}H_{16}N_2O_6$	7.61	8.03
37	$4\text{-}C_2H_5O\text{-}3\text{-}CH_3OC_6H_3-$	$o\text{-}NO_2C_6H_4-$	33[e,h]	162	$C_{19}H_{16}N_2O_6$	7.61	8.03
38	$4\text{-}C_2H_5O\text{-}3\text{-}CH_3OC_6H_3-$	$m\text{-}NO_2C_6H_4-$	69[b,e]	206	$C_{19}H_{16}N_2O_6$	7.61	7.96
39	$4\text{-}C_2H_5O\text{-}3\text{-}CH_3OC_6H_3-$	$p\text{-}NO_2C_6H_4-$	73[e,i]	213	$C_{19}H_{16}N_2O_6$	7.61	8.05
41	$3,4\text{-}(C_2H_5O)_2C_6H_3-$	$o\text{-}NO_2C_6H_4-$	34[d,h]	167	$C_{20}H_{18}N_2O_6$	7.33	7.76
42	$3,4\text{-}(C_2H_5O)_2C_6H_3-$	$m\text{-}NO_2C_6H_4-$	69[b,f]	166	$C_{20}H_{18}N_2O_6$	7.33	7.73
43	$3,4\text{-}(C_2H_5O)_2C_6H_3-$	$p\text{-}NO_2C_6H_4-$	71[b,i]	220	$C_{20}H_{18}N_2O_6$	7.33	7.65
45	$3,4\text{-}CH_2O_2C_6H_3-$	$o\text{-}NO_2C_6H_4-$	35[b,h]	188	$C_{17}H_{10}N_2O_6$	8.28	8.57
46	$3,4\text{-}CH_2O_2CH_3-$	$m\text{-}NO_2C_6H_4-$	69[e,f]	196	$C_{17}H_{10}N_2O_6$	8.28	8.28
47	$3,4\text{-}CH_2O_2C_6H_3-$	$p\text{-}NO_2C_6H_4-$	71[d,h]	245	$C_{17}H_{10}N_2O_6$	8.28	8.36
49	$3,4,5\text{-}(CH_3O)_3C_6H_2-$	$o\text{-}NO_2C_6H_4-$	28[b,h]	209	$C_{17}H_{16}N_2O_7$	7.29	7.55
50	$3,4,5\text{-}(CH_3O)_3C_6H_2-$	$m\text{-}NO_2C_6H_4-$	50[b,e]	219	$C_{19}H_{16}N_2O_7$	7.29	7.32
51	$3,4,5\text{-}(CH_3O)_3C_6H_2-$	$p\text{-}NO_2C_6H_4-$	54[b,h]	230	$C_{19}H_{16}N_2O_7$	7.29	7.27
53	$4\text{-}CH_3COO\text{-}3\text{-}CH_3OC_6H_3-$	$o\text{-}NO_2C_6H_4-$	51[b,f]	190	$C_{19}H_{14}N_2O_7$	7.33	7.34
54	$4\text{-}CH_3COO\text{-}3\text{-}CH_3OC_6H_3-$	$m\text{-}NO_2C_6H_4-$	58[b,f]	209	$C_{19}H_{14}N_2O_7$	7.33	7.69
55	$4\text{-}CH_3COO\text{-}3\text{-}CH_3OC_6H_3-$	$p\text{-}NO_2C_6H_4-$	71[b,h]	215	$C_{19}H_{14}N_2O_7$	7.33	7.04
57	$3\text{-}CH_3COO\text{-}4\text{-}CH_3OC_6H_3-$	$o\text{-}NO_2C_6H_4-$	21[e,h]	169	$C_{19}H_{14}N_2O_7$	7.33	7.79
58	$3\text{-}CH_3COO\text{-}4\text{-}CH_3OC_6H_3-$	$m\text{-}NO_2C_6H_4-$	57[d,f]	182	$C_{19}H_{14}N_2O_7$	7.33	7.77
59	$3\text{-}CH_3COO\text{-}4\text{-}CH_3OC_6H_3-$	$p\text{-}NO_2C_6H_4-$	67[e,h]	199	$C_{19}H_{14}N_2O_7$	7.33	7.70
61	$o\text{-}NO_2C_6H_4-$	$o\text{-}NO_2C_6H_4-$	57[b,f]	210	$C_{16}H_9N_3O_6$	12.38	12.37
62	$o\text{-}NO_2C_6H_4-$	$m\text{-}NO_2C_6H_4-$	36[e,f]	196	$C_{16}H_9N_3O_6$	12.38	12.45
63	$o\text{-}NO_2C_6H_4-$	$p\text{-}NO_2C_6H_4-$	71[b,f]	237	$C_{16}H_9N_3O_6$	12.38	12.34
65	$m\text{-}NO_2C_6H_4-$	$o\text{-}NO_2C_6H_4-$	60[e,f]	188	$C_{16}H_9N_3O_6$	12.38	12.46
66	$m\text{-}NO_2C_6H_4-$	$m\text{-}NO_2C_6H_4-$	83[b,e]	243	$C_{16}H_9N_3O_6$	12.38	12.16
67	$m\text{-}NO_2C_6H_4-$	$p\text{-}NO_2C_6H_4-$	85[b,f]	258	$C_{16}H_9N_3O_6$	12.38	12.02
69	$p\text{-}NO_2C_6H_4-$	$o\text{-}NO_2C_6H_4-$	50[b,f]	248	$C_{16}H_9N_3O_6$	12.38	12.39
70	$p\text{-}NO_2C_6H_4-$	$m\text{-}NO_2C_6H_4-$	72[b,f]	251	$C_{16}H_9N_3O_6$	12.38	12.56
71	$p\text{-}NO_2C_6H_4-$	$p\text{-}NO_2C_6H_4-$	60[b,f]	295	$C_{16}H_9N_3O_6$	12.38	12.68

[a] Numbers refer to same compounds as in Table I. [b] Needles. [e] Prisms. [d] Plates. [e] Pale yellow. [f] Yellow. [g] Yellow orange. [h] Orange. [i] Red.

ences in activity are narrowed. For instance, when an azlactone has a $m\text{-}CH_3O-$ group in R_1 (No. 9), its first maximum is at 366 mμ and when a $p\text{-}NO_2-$ group is present in R_1 (No. 68), its first maximum is at 376 mμ with a difference of 10 mμ. But when an $o\text{-}NO_2$ group is simultaneously present in R_2 each azlactone (No. 10 and 69), gives a maximum at the same wave length of 375 mμ.

This equalization of the shifts results from the interaction of the two groups, $o\text{-}NO_2-$ and $p\text{-}NO_2-$, which have the same mesomeric effect and are united through a conjugated system. This inter-

action will be discussed later for a similar case where two p-NO_2 groups one in R_1 the other in R_2 are present.

When the substituent in R_2 is a m-NO_2 group, the order of activity for the substituents in R_1 is maintained with two exceptions. The orders m-CH_3O- > p-CH_3COO- and o-NO_2- > m-NO_2- found when R_2 is unsubstituted are reversed (compare, No. 9 and 20 with 11 and 22 and No. 60 and 64 with 62 and 66.) These inversions are determined by small differences in the first maximum, and no particular reason can be given for determining same.

When a p-NO_2- group is placed in R_2, the order of activities o-CH_3O- > p-CH_3O- and p-NO_2- > m-CH_3O-, found for simple substitution in R_1 are also reversed (compare No. 5 and 13 with 8 and 16, and No. 9 and 68 with 12 and 71). These inversions result from the interaction of the two substituents.

In the azlactones with an o-CH_3O- or a p-CH_3O- in R_1 and a p-NO_2- in R_2, an electron-donating and an electron-attracting substituent are united through a conjugated system of double bonds and phenyls. The positions of the substituents allow for an interaction of their mesomeric effects, through the conjugated system. It is known that substitutions of this type, by action on the π electrons, determine a shift on the absorption maximum to longer wave lengths in relation to the unsubstituted structure.[16]

For example, the unsubstituted azlactone has a maximum at 361 mμ (No. 1), which can be displaced to 409 mμ, by introducing a p-NO_2- into R_2 and an o-CH_3O- into R_1 (No. 8); and to 411 mμ by introducing a p-CH_3O- into R_1 (No. 16). The conjugated system p-CH_3O-:p-NO_2- is longer than o-CH_3O-:p-NO_2-, and consequently the azlactone No. 16 has a maximum at longer wave lengths than azlactone No. 8. When there is no p-NO_2- in R_2, the azlactone with an o-CH_3O- in R_1 (No. 5) has a maximum at 386 mμ while with a p-CH_3O- present in R_1 (No. 13), the maximum is at 383 mμ. The difference is small, and one explanation for the greater activity of the o-CH_3O- group may be found in the fact that it can transmit its mesomeric effect easier to the remaining conjugated system better than the p-CH_3O-, since it is placed nearer to the phenyl conjugated double bond that relays it to the remaining components of the system.

The conjugated system is shorter in the case of the o-CH_3O- than for the p-CH_3O, but it is evident that the mobility of the π-electrons is greater for

the former substitution than for the latter and the maximum of azlactone No. 5 is found at a longer wave length than for azlactone No. 13.

The inversion of activities of groups p-NO_2- and m-CH_3O-, when the spectra of azlactones with only those substituents in R_1 (No. 9 and 68) are compared with azlactones that have also a p-NO_2- in R_2 (No. 12 and 71), is the result of the low bathochromic effect of the two p-NO_2- in azlactone 71, because they are placed at the ends of the conjugated system.

This partial neutralization of the bathochromic activity of identical substituents, when they are united through a conjugated system, has already been observed.[16] It is a result of their identical mesomeric effect that works in opposed direction and decreases the mobility of the π-electrons.

As a result, azlactone 71 has a maximum at 383 mμ, located at shorter wave lengths than when a m-CH_3O- is present in R_1 and a p-NO_2 in R_2 (No. 12, λ_{max} 387 mμ). The order of activity of the substituents in R_1 is m-CH_3O- > p-NO_2-.

When there is no substituent in R_2, the p-NO_2- group in R_1 exerts a stronger mesomeric effect than the m-CH_3O-, and the maximum for the former azlactone (No. 68) is at 376 mμ, while for the latter (No. 9) is at 366 mμ and the order of activity is p-NO_2- > m-CH_3O-.

Experimental

Determination of the Absorption Spectra.—The absorption spectra were determined with a Beckman spectrophotometer model DU employing silica cells 1 cm. wide.

The spectrophotometer was checked and correct values found for the sodium line at 589 mμ and α hydrogen line at 656 mμ. Correct values were also obtained for the transmission and absorption of a potassium chromate solution prepared according to Haupt.[17] The spectra were determined in acetic acid and ethanol in 0.00005 M solution.

Preparation of the Azlactones.—All the known azlactones were prepared according to literature data.[18] The azlactones derived from the nitrohippuric acids were new and the following method was used. In a test-tube with a condenser, 1.07 millimoles of the hippuric acid, 0.96 millimole of the aromatic aldehyde, 0.96 millimole of fused sodium acetate and 3 millimoles of acetic anhydride, were well mixed and heated in a boiling water-bath for one hour. After cooling, 2 ml. of 96% ethanol was added to the contents of the test-tube, the mixture left at 5° for 4–6 hours and the precipitate formed filtered, washed with cold ethanol, then with boiling water and again with cold ethanol. The dried precipitate was recrystallized to constant melting point in acetic acid.

The yields, crystalline form, color, melting points and analysis of the new azlactones, are reported in Table II.

BUENOS AIRES, ARGENTINA

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