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The Synthesis and Color of Pyrido[1′,2′ : 1,2]pyrimido[4,5-*b*]acridine-7,15-diones

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Some derivatives of pyrido[1′,2′: 1, 2]pyrimido[4,5-*b*]acridine-7,15-diones have been synthesized, their absorption spectra have also been investigated in order to elucidate the relationship between the color and the chemical constitution in contrast to the related compounds, quinacridone and pyrido[2,1-*b*]pyrido[1′,2′ : 1,2]pyrimido-[4,5-*g*]quinazoline-7,15-dione. The absorption spectra in DMSO and in concentrated sulfuric acid show a good correlation with the electronic effect of the substituents. The absorption spectra of the solid are more influenced by the position of the substituents than by the electronic effect.

Linear *trans*-quinacridone (**1**) is a valuable organic pigment because of its excellent properties. Therefore, much attention has heen paid to the synthesis and the electronic spectral studies of quinacridones and some derivatives with similar chemical constitutions.[1] The substituents of quinacridones have little effect on the visible spectra in concentrated sulfuric acid, but a marked effect on the solid color.[2] In a previous paper, we showed that the introduction of methyl groups into the 1,9- and 4,12-positions of pyrido[2,1-*b*]pyrido[1′,2′ : 1,2]pyrimido[4,5-*g*]quinazoline-7,15-dione (**2**) gives rise to a hypsochromic shift from red to orange in the solid color.[3] Altiparmakin has reported that the effect of the substituents of **2** on the electronic spectra is practically negligible in contrast to the case of **1**, since the substituents are, in fact, isolated from chromophore.[4]

It is interesting to make clear the relationship between the color and the chemical constitution of those compounds. Therefore, in this study, some derivatives of 5*H*-pyrido[1′,2′:1,2]pyrimido[4, 5-*b*]acridine-7,15-dione (**3a**) were synthesized, and their electronic spectra in solutions and their reflectance spectra in the solid were compared with those of **1** and **2**.

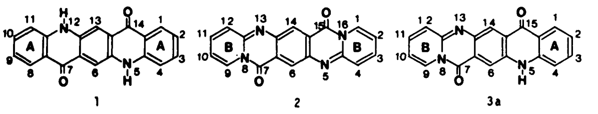


Fig. 1.

Experimental

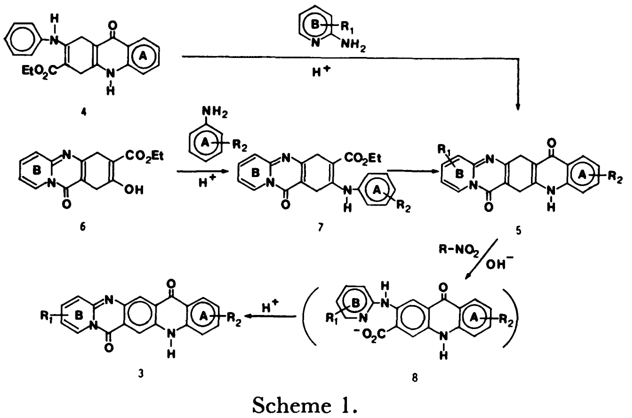
The IR, VS, and ^{1}H-NMR spectra were recorded on a Shimadzu IR-27G spectrophotometer, a Hitachi 306 spectrophotometer, and a Varian HA-100 spectrometer respectively. The color measurements were obtained using a Hitachi Trichromatic Integrator.

Materials. All the reagents except those listed below were obtained from commercial sources and were used without further purification.

Improved methods for the preparation of **3a** were employed to obtain substituted **3**, whose A or B ring carries substituents (Scheme 1).

The synthetic intermediates, 2-anilino-3-ethoxycarbonyl-1,4-dihydro-9(10*H*)-acridone (**4**) and 7-ethoxycarbonyl-6,9-dihydro-8-hydroxypyrido[2,1-*b*]quinazolin-10-one (**6**) were prepared according to the methods described in the literature.[5]

*6, 14-Dihydropyrido[1′, 2′ : 1, 2]pyrimido[4, 5-*b*]acridine-7, 15-diones (5).* *a)*: The reaction of **4** and 2-aminopyridines were carried out according to the methods described in a previous paper.[4] Pale pink solids of **5a**—**e** were obtained.



Scheme 1.

b): A mixture of 5.0 g, of **6** and 19 g of *p*-toluidine was heated to reflux in 50 ml of acetic acid for 2.5 h while being stirred under a nitrogen atmosphere. When the reddish orange solution was then cooled, a pale orange solid precipitated. The solid was collected on a filter, washed with methanol, and dried at 60 °C. The solid (5.0 g) was heated in 70 g of polyphosphoric acid for 1 h. The resulting solution was diluted with large excess of water to give **5f** as a pale pink solid. The other substituted derivatives were prepared analogously.

In this reaction, the methoxyl-group at the 2-position of **5** was hydrolyzed to the 2-hydroxy derivative **5h**. The methoxyl-group at the 4-position of **5** was not hydrolyzed under the same reaction conditions. Some pertinent data on **5** are also shown in Table 1.

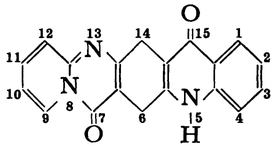
*Pyrido[1′,2′ : 1,2]pyrimido[4,5-*b*]acridine-7,15-diones (3).* *a)*: The dehydrogenation of **5** was carried out, using sodium *m*-nitrobenzenesulfonate as a dehydrogenating agent, by the method described in our previous paper.[6]

b): A mixture of 5.0 g of **5b**, 5.0 g of sodium *m*-nitrobenzenesulfonate, 9 g of a 33% aqueous sodium hydroxide solution, and 100 g of ethylene glycol was heated at 100—130 °C for 2 h. The resulting red solution was cooled and neutralized with an aqueous sulfuric acid solution. The precipitate was filtered, washed with water, and dried at 60 °C.

Three grams of the brown colored powder were heated at 90—100 °C for 2 h in 50 g of polyphosphoric acid. The resulting red solution was cooled to room temperature and then diluted with 200 ml of water. The reddish orange crystals thus precipitated were filtered, washed with water, and dried at 60 °C. The yield was 2.3 g (76.7%).

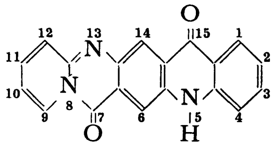
The compounds **3** were conveniently purified by the following procedure. To a suspension of 3 g of crude **3a**—**l** in 100

TABLE 1. 6,14-DIHYDROPYRIDO [1′,2′ : 1,2] PYRIMIDO [4,5-*b*] ACRIDINE-7,15-DIONES



5	Substituent position	Yield %	Found (%) C	Found (%) H	Found (%) N	Calcd (%) C	Calcd (%) H	Calcd (%) N	IR (KBr) ν_{N-H}/cm^{-1}	ν_{C-O}/cm^{-1}	
5a	None	85	72.41	4.32	13.22	72.37	4.15	13.33	3270	1670	1640
5b	9-CH_3	72.5	73.08	4.65	13.02	72.92	4.60	12.76	3270	1668	1640
5c	10-CH_3	98.0	72.79	4.36	12.93	72.92	4.60	12.76	3270	1720	1665
5d	11-CH_3	92.2	72.50	5.07	12.63	72.92	4.60	12.76	3270	1678	1640
5e	12-CH_3	84.0	73.20	4.76	12.48	72.92	4.60	12.76	3280	1680	1640
5f	2-Cl	94.1	65.05	3.62	12.19	65.24	3.46	12.02	3280	1725	1670
5g	2-CH_3	97.0	72.76	4.33	12.90	72.92	4.60	12.76	3280	1725	1675
5h	2-OH	97.7	69.47	4.03	12.60	68.88	3.93	12.69	3280	1725	1670
5i	2-$COCH_3$	92.8	70.41	4.37	11.86	70.59	4.20	11.76	3280	1725	1670
5j	4-CH_3	86.2	73.16	4.90	12.47	72.92	4.20	12.76	3250	1730	1675
5k	4-OCH_3	86.2	69.04	4.61	12.18	69.55	4.39	12.17	3280	1720	1670
5l	4-Cl	93.0	65.52	3.57	11.89	65.24	3.46	12.02	3280	1690	1670

TABLE 2. PYRIDO [1′,2′ : 1,2] PYRIMIDO [4,5-*b*] ACRIDINE-7,15-DIONES



3	Substituent position	Yield %	Found (%) C	Found (%) H	Found (%) N	Calcd (%) C	Calcd (%) H	Calcd (%) N	IR (KBr) ν_{N-H}/cm^{-1}	$\nu_{C=O}$/cm^{-1}	
3a	None	95.5	72.31	3.74	13.22	72.84	3.54	13.41	3260	1700	1650
3b	9-CH_3	76.7	73.28	4.44	12.86	73.37	4.01	12.84	3250	1710	1660
3c	10-CH_3	90.7	73.86	4.02	12.59	73.37	4.01	12.84	3320	1730	1680
3d	11-CH_3	97.9	73.69	4.27	12.85	73.37	4.01	12.84	3280	1725	1655
3e	12-CH_3	97.2	73.48	4.00	12.58	73.37	4.01	12.84	3250	1690	1650
3f	2-Cl	97.5	65.11	3.69	12.27	65.62	3.49	12.09	3280	1740	1650
3g	2-CH_3	95.9	73.85	4.43	12.96	73.37	4.01	12.84	3250	1740	1650
3h	2-OH	89.4	69.54	4.12	12.70	69.30	3.34	12.77	3250	1740	1650
3i	2-$COCH_3$	93.9	70.61	3.75	11.84	70.99	3.66	11.83	3250	1740	1650
3j	4-CH_3	94.1	73.27	4.18	12.76	73.37	4.01	12.84	3250	1700	1650
3k	4-OCH_3	88.5	69.34	3.92	12.49	69.96	3.82	12.24	3350	1700	1650
3l	4-Cl	96.8	65.31	3.57	12.01	65.62	3.49	12.09	3330	1690	1653

ml of ethylene glycol we added 10 g of a 20% aqueous sodium hydroxide solution. The mixture was heated with continuous stirring at 100—120 °C for 2 h. The resulting red solution was cooled and acidified with 20 g of a 20% aqueous sulfuric acid solution. The slurry thus formed was heated at 70—80 °C for 1 h. The product was collected by filtration and washed with hot ethylene glycol and then water. Recrystallization from DMSO afforded reddish orange crystals (2.7 g, 90% recovery).

The yields and some pertinent data for **3** are listed in Table 2.

Picrate. *a)*: A mixture of 100 ml of ethanol, 2.0 g of **2**, and 5.0 g of picric acid was heated to reflux for 2 h. The resultant yellow solid was collected by filtration, washed with ethanol, and dried at 60 °C. The yield was 4.2 g. The product was determined to be picrate (**2** : picric acid = 1 : 2, M/M, 1 M = 1 mol dm^{-3}) by means of IR spectroscopy and elemental analysis. Found: C; 47.09, H; 2.24, N; 18.29%. Calcd for $C_{30}H_{16}N_{10}O_{16}$: C; 46.64, H; 2.09, 18.13%. IR (KBr) C=O 1705 cm^{-1}. *b)*: From 2.0 g of **3a** and 5.0 g of picric acid, 3.4 g of orange crystals were obtained by means of the procedure described above. The product was determined to be picrate (**3a**: picric acid = 1 : 1, M/M) by IR spectroscopy and elemental analysis. Found: C; 55.51, H; 2.50, N; 15.96%. Calcd for $C_{25}H_{14}N_6O_9$; C; 55.35, H; 2.58, N; 15.50%. IR(KBr) C=O 1723 cm^{-1}. *c)*: The 4,12-dimethyl derivative of **2** and the 4-methyl derivative of **3a**(**3e**) formed no picrate.

Color Measurements. The visible absorption maxima of the solid were obtained from the reflectance spectra on the dispersion of the solid diluted with TiO_2(1/5) in cellulose acetate butyrate.

Spectral Measurements. The visible spectra of **1**, **2**, and **3** were measured on both DMSO and concentrated sulfuric acid solutions, ranging in concentration from 1×10^{-3} to 1×10^{-5} M. The spectra were independent of the concentration in this concentration range.

TABLE 3. ^{1}H-NMR DATA FOR **1**, **2**, AND **3** IN CONCD H_2SO_4

Compound		Chemical shifts δ										
		H_1	H_2	H_3	H_4	H_8	H_9	H_{10}		H_{11}		$H_{6,13}$
1		9.14	8.42	8.88	8.65	9.14	8.42	8.88		8.65		10.08
		H_1	H_2	H_3	H_4	H_9	H_{10}	H_{11}	H_{12}	H_5	H_6	H_{14}
2		9.83	8.33	9.12	8.52	9.83	8.33	9.12	8.52		9.48	9.48
3a		9.03	8.51	8.94	8.73	9.72	8.25	9.14	8.47	12.96	9.93	9.61
3b	9-CH_3	9.18	8.51	8.8	8.8	$CH_3$3.75	7.92	8.8	8.22	12.88	9.77	9.44
3c	10-CH_3	9.16	8.48	8.91	8.70	9.56	$CH_3$3.10	8.90	8.38	12.92	9.87	9.56
3d	11-CH_3	9.18	8.50	8.92	8.71	9.64	8.06	$CH_3$3.30	8.21	12.93	9.89	9.55
3e	12-CH_3	9.16	8.50	8.9	8.70	9.70	8.17	8.9	$CH_3$3.35	12.94	9.89	9.84
3f	2-Cl	9.10	—	8.83	8.7	9.88	8.24	9.04	8.50	13.11	9.93	9.56
3g	2-CH_3	8.92	$CH_3$3.25	8.88	8.64	9.77	8.24	9.06	8.46	12.93	9.90	9.58
3h	2-OH	8.97	—	8.87	8.74	9.77	8.24	9.06	8.45	13.24	9.95	9.52
3i	2-$COCH_3$	9.1	$COCH_3$4.0	9.0	8.8	9.8	8.3	9.4	8.5	13.30	9.95	9.63
3j	4-CH_3	9.02	8.4	8.75	$CH_3$4.46	9.77	8.23	9.0	8.4	12.34	10.13	9.57
3k	4-OCH_3	9.0	8.40	8.67	$OCH_3$4.80	9.76	8.18	9.04	8.44	13.11	10.05	9.57
3l	4-Cl	8.98	8.46	9.20	—	9.79	8.26	9.08	8.47	12.73	10.18	9.60

Compound	Coupling constants/Hz
1	$J_{1,2}=J_{8,9}=8.0$ $J_{1,3}=J_{8,10}=1.6$ $J_{1,4}=J_{8,11}=0$ $J_{2,3}=J_{9,10}=6.8$ $J_{2,4}=J_{9,11}=1.4$ $J_{3,4}=J_{10,11}=8.2$
2	$J_{1,2}=J_{9,10}=6.8$ $J_{1,3}=J_{9,11}=1.2$ $J_{1,4}=J_{9,12}=0$ $J_{2,3}=J_{10,11}=7.4$ $J_{2,4}=J_{10,12}=0.8$ $J_{3,4}=J_{11,12}=8.0$
3a	$J_{1,2}=8$ $J_{1,3}=1.6$ $J_{1,4}=0$ $J_{2,3}=8$ $J_{2,4}=1.4$ $J_{3,4}=8.4$ $J_{9,10}=7.2$ $J_{9,11}=0.7$ $J_{9,12}=0$ $J_{10,11}=8$ $J_{10,12}=0.8$ $J_{11,12}=8$

TABLE 4. VISIBLE SPECTRA FOR **1**, **2**, AND **3**

Compound	Substituent	Solid color λ/nm[a]				Solution, in DMSO λ/nm (ε)			in concd H_2SO_4 λ/nm (ε)		
		λ_1	λ_2	λ_3	λ_d[b]	λ_1	λ_2	λ_3	λ_1	λ_2	λ_3
1	H	490	525	560	λ_c 500	462 (3600)	491 (10000)	525 (16000)	517 (4500)	556 (9500)	597 (11500)
2	H	484	516	560	620	458 (4000)	487 (8000)	519 (6000)	420 (3800)	437 (7500)	469 (7500)
3a	H	468	495	523	603	460 (5000)	487 (9200)	519 (9700)	450 (5500)	483 (9000)	516 (8400)
3b	9-CH_3	470s[c]	503	535s	597	460 (3900)	487 (4900)	519 (4400)	458 (3400)	486 (5400)	519 (5100)
3c	10-CH_3	474	502	535	614	460 (5300)	487 (8800)	520 (8800)	455 (3100)	489 (6200)	522 (6200)
3d	11-CH_3	475	505	537	615	462 (4300)	489 (7300)	522 (7400)	455 (4880)	485 (6600)	517 (6200)
3e	12-CH_3	478	507	537	615	459 (4700)	486 (8200)	517 (8500)	455 (3800)	486 (5100)	518 (4800)
3f	2-Cl	485	517	551	λ_c 493	464 (4800)	491 (8000)	524 (8300)	460 (2500)	488 (4300)	521 (4000)
3g	2-CH_3	485	519	552	644	464 (4600)	492 (8000)	525 (8500)	460 (2600)	488 (4600)	520 (4600)
3h	2-OH	480s	512	542s	λ_c 493	464 (3200)	494 (5700)	528 (6100)	452 (4000)	481 (6700)	513 (6400)
3i	2-$COCH_3$	474	505	540	614	452 (5400)	480 (8000)	511 (7500)	464 (4200)	497 (4500)	530 (3900)
3j	4-CH_3	465	490	524	588	458 (4700)	485 (8100)	517 (8100)	460 (4600)	487 (7200)	520 (6700)
3k	4-OCH_3	470	496	530	602	460 (5000)	488 (8200)	520 (8200)	455 (3300)	482 (5500)	513 (5900)
3l	4-Cl	465	493	526	594	456 (5000)	483 (8300)	515 (8300)	463 (4500)	490 (7300)	523 (6900)

a) Obtained from a reflectance spectrum on a dispersion of a solid diluted with TiO_2(1/5) in CAB resin film. b) λ_d shows the dominant wave length, while λ_c represents the complementary wavelength. They were obtained from the C.I.E. Chromaticity Diagram by using Tristimulas Values available from the integration of the reflectance spectra with a trichromatic integrator. c) Shoulder.

Results and Discussion

Dihydro derivatives **5** were synthesized according to the two methods previously reported,[6] as is shown in Scheme 1. The first method gives **5** directly. Amine exchange and intramolecular cyclization spontaneously occurred on the heating of **4** with substituted amino pyridines in acetic acid. The second method involved the preparation of esters **7**, which were obtained by the condensation of **6** with substituted anilines. The cyclization of **7** was carried out in polyphosphoric acid. In this reaction, the *p*-methoxy group (R_2=*p*-OCH_3) of **7** was hydrolyzed to give 2-hydroxy derivative (**5h**), but the *o*-methoxy group was not hydrolyzed under the same reaction conditions. The dehydrogenation of **5** gave the corresponding **3** in high yields.

The compounds **3** are microcrystalline powders and range from orange to red in color. They do not melt or decompose up to 300 °C and are slightly soluble in organic solvents, such as dimethylformamido and dimethylsulfoxide (DMSO). The compounds **3**, as well as compound **2**, are weak bases and are soluble in aqueous solutions of strong acids, such as hydrochloric acid and sulfuric acid. The compounds **2** and **3** formed picrates, the 1 : 2 adduct of **2** and the 1 : 1 adduct of **3** with picric acid. However, the 4,12-dimethyl derivative of **2** and the 4-methyl derivative of **3a**(**3e**) formed no picrate. This is probably due to the steric hindrance between the methyl group adjacent to imino nitrogen and the voluminous nitro group of picric acid.

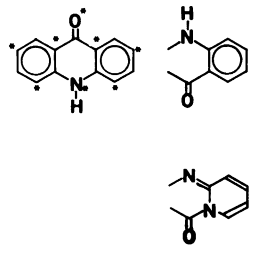
The absorption spectra of **3** were measured and compared with those of **1** and **2** in order to clarify the influences of substituents and of the measurement medium upon the electronic spectra. The ^{1}H-NMR data for **1**, **2**, and **3** are listed in Table 3. The coupling pattern of **2** is similar to that of **1**, but the proton signals of **2** are distributed over a wider range than those of **1**. The coupling constants for **2** are slightly smaller than those of **1**. The spectra of **3** appear almost as a superimposition of those of **1** and **2**. The chemical shifts of the aromatic protons of **3** are scarcely influenced by the electronic effects of their substituents.

The visible absorption spectra of **1**, **2**, and **3** in various media are listed in Table 4. The compounds **1** and **2** show visible absorptions at considerably shorter wavelengths in DMSO than in a solid. However, in concentrated sulfuric acid the spectrum of **1** shows a strong bathochromic shift, and that of **2**, a remarkable hypsochromic shift. On the other hand, the spectrum of **3a** is little affected by either solvent.

The strong bathochromic shift of **1** in concentrated sulfuric acid can be explained by the increased acceptor capacity of the carbonyl group for the protonation on the carbonyl oxygens. The hypsochromic shift of **2** in concentrated sulfuric acid may be attributed to the protonation at the imino nitrogens.[7] The imino protonation will destroy the polymethine chromophore. In the case of **3**, the bathochromic effect of the protonated acridone skeleton is counteracted by the protonation of the quinazolone skeleton, and the spectral shift is, consequently, small.

These spectral shifts can be interpreted on the basis of the assumption of protonated species, as is shown in Fig. 2. The protonated species **14** and **12** are regarded as the aza-replaced compounds of **1** and its mono protonated structure, **9**, respectively. The aza replacement at the 7a and 14a positions of **1** shows a remarkable hypsochromic shift. The observed shift is in accordance with the color rules.[8]

The compound **3a** absorbs at shorter wavelengths than **1**. This can easily be explained in terms of the replacement of an electron-donor substituent, NH, with an electron-accepter substituent, C=N, at the starred position of an acridone molecule.



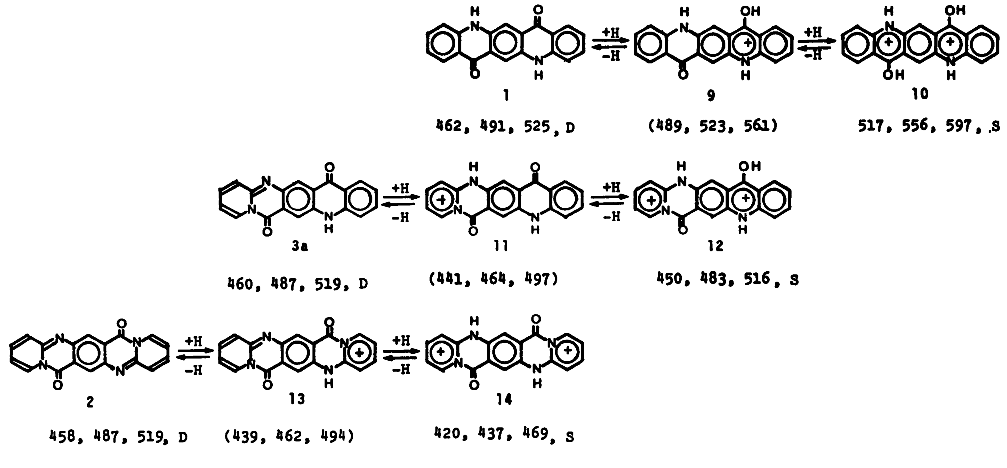


Fig. 2. Structure and spectral wavelength of compounds **1**, **2**, and **3** and their assumed protonated speacies, λ_{max}, (speculated values), nm. D: in DMSO, S: in concentrated sulfuric acid.

In the case of the substituted derivatives of **3a**, it is predictable that an electron-donating substituent at the starred position will show a bathochromic effect. The observed visible spectra of the derivatives of **3a** in the solutions show a good correlation with the electronic effect of the substituents, though the effect is small. Electron-donating substituents cause a bathochromic effect in DMSO and a hypsochromic effect in concentrated sulfuric acid. The substituent effect on protonated **3** is opposed to that on the unprotonated species. The opposite wavelength shifts by the protonation are not observed in the substituents of **1**. The observed wavelength shifts of **3** give straight-line relationship with Hammett σ constants, as is shown in Fig. 3. The relationship to the reactive substituent constant is explained by the fact that the shifts are closely related to the protonation equilibria of **3**. That is, the electron-donating substituents increase the donating ability of the acridone NH group, hence, the bathochromic shift is observed in DMSO. On the other hand, the electron-acceptor groups accelerate the protonation of the acridone skeleton, and the bathochromic shift is observed in concentrated sulfuric acid.

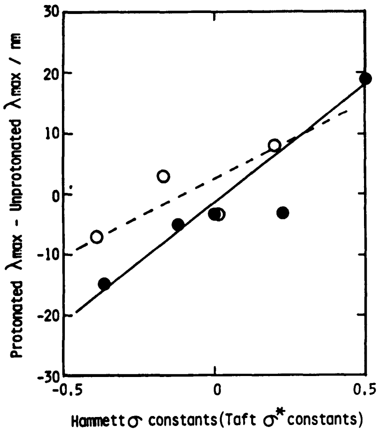


Fig. 3. Spectral longest-wavelength shifts observed with the protonation of **3** plotted against Hammett σ constants (para) ——, and Taft σ^* constants (ortho) …….

The substituents of **3** show a pronounced effect on their solid colors. The shades of the solid are also listed in Table 4 in terms of the dominant wavelength values, λ_d or λ_c. The substituents at the 2-position exert a bathochromic effect. The shift is larger than that in DMSO, but shows a poor correlation with the electronic effect of the substituents. The substituents at the 4-position exert almost no effect, and the λ_{max} values are almost the same as those of unsubstituted **3a** either in a solid or in DMSO. The 9, 10, 11, and 12-methyl substituted derivatives absorb light of wavelengths longer than **3a**, but the shift is smaller than that of the 2-methyl substituted derivative, **3g**. On the basis of this spectroscopy, the following conclusions were deduced: the effect of the substituent on the A ring of **3** upon the absorption spectra is larger than that of the substituent on the B ring, and the absorption spectra are more influenced by the position of the substituent than by the electronic effect of the substituent.

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