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Substituent Effects and Structural Limitations in the Conversion of 3,3-Diarylphthalides to 4,4-Diaryl-3,4-dihydro-1(2*H*)-phthalazinones

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Heating of crystal violet lactone (CVL) (**1a**) and its analogs with hydrazine hydrate afforded a single product in each case, to which the 4,4-diaryl-3,4-dihydro-1(2*H*)-phthalazinone structure (**2**) was assigned.

Kinetic data showed that the introduction of a dimethylamino substituent in 3,3-diarylphthalides (**1**) led to an increase in the rate of formation of the dihydrophthalazinone (**2**). Thus, the reaction seems to occur by a mechanism which involves a carbonium intermediate. Replacement of 3,3-diaryl groups on the phthalide by a xanthyl group resulted in the formation of an N-aminophthalimidine derivative on similar treatment. The dihydrophthalazinone (**2a**) exhibited a greenish-blue color on exposure to a weak acid, indicative of heterolytic ring cleavage to form the dye cation, whereas treatment of **2a** with a strong acid resulted in a facile conversion to the N-aminophthalimidine (**6**) and CVL (**1a**) in a ratio of *ca.* 2 : 1.

Keywords——dihydrophthalazinone; N-aminophthalimidine; triaryl carbocation; substituent effect; structural limitation; lactone-ring opening; light sensitive leuco-dye

It has been known for many years that 3,3-(*p*-dimethylaminophenyl)-6-dimethylaminophthalide (**1a**) [crystal violet lactone (CVL)] and 3,3-bis-*p*-dimethylaminophenylphthalide (**1b**) [malachite green lactone (MGL)] readily undergo heterolytic cleavage of the lactone ring to form the intensely colored dye-cation on exposure to appropriate weak acids, *i.e.*, electrophilic reagents.[2)] The resonance formulation of the extensively delocalized colored dye, as shown in Chart 1 for MGL (**1b**) as an example, involves the carbocations (1a), and the equi-

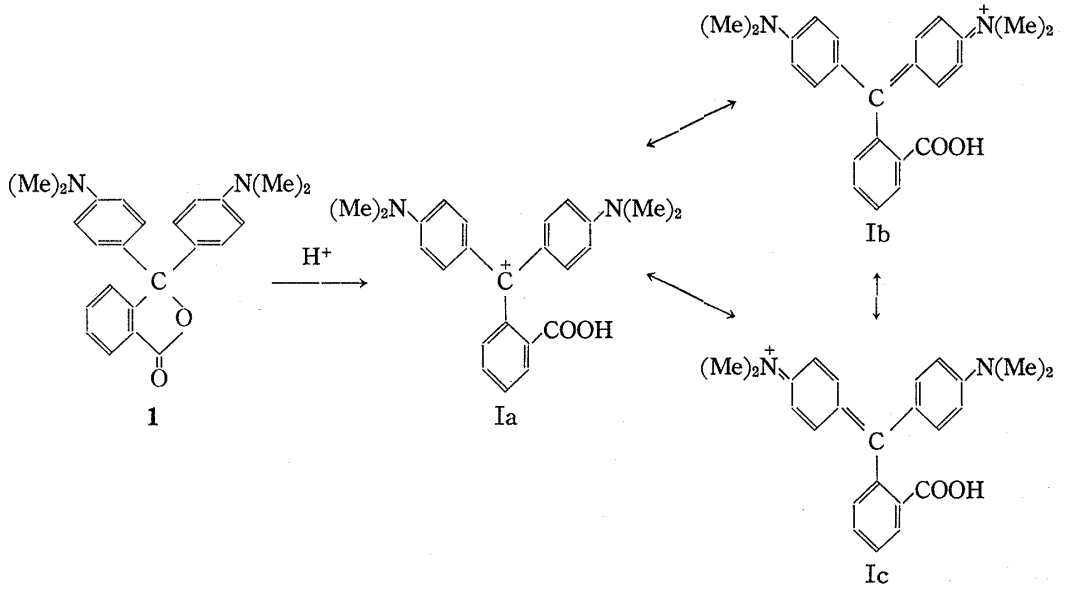


Chart 1

1) Location: *5-6-1, Mitahora-Higashi, Gifu, 502, Japan.*
2) G. Kortum and J. Vogel, *Chem. Ber.*, **93**, 706 (1960).

valent quinoid-immonium ions (1b)—(1c).

These coloration processes have been the object of extensive studies, and various reports concerned with the syntheses of their derivatives and with their coloration properties have been published.[3] Many of the previous investigations deal mainly with variations of the substituents on the benzene ring. In addition, the reactions and reaction kinetics of triphenyl carbocations including dye cations with various nucleophiles such as hydrazines, cyanide, thiol, alkoxyl and hydroxyl anions were intensively investigated as part of a series of studies on the nature of stable carbocations and their structure-reactivity relationship,[4] and there has been interest in their photochromic behavior.[5]

On the other hand, the reaction of 3,3-diarylphthalides with nucleophiles to alter the lactone ring has received only very limited attention, although heating of phenolphthalein and its methoxy derivatives with hydrazine was shown to give the corresponding 4,4-diaryl-3,4-dihydro-1(2*H*)-phthalazinones in moderate yields.[6] However, phenolphthalein, unlike CVL and MGL, has long been known to undergo ring-opening readily to produce a red color in basic media due to an acidic functional hydroxy group. The reaction of CVL or MGL with hydrazine, therefore, should be considered as distinct from that of phenolphthalein.

Furthermore, there has been very little work done on the chemistry of 4,4-disubstituted-3,4-dihydro-1(2*H*)-phthalazinones; these are among the expected products in such reactions which seem to involve many potentially interesting features, such as (a) the possible development of new types of leuco precursor for colored dyes, including modifications of such compounds; (b) the photochemical behavior in ring opening; (c) the nature and reactivity of the hitherto unknown six-membered α-monocarbonyl azo-compounds formally obtainable by oxidation.

In view of these points of interest, this work has been undertaken to define the scope and limitations of the reaction of 3,3-diarylphthalides with hydrazines and to elaborate the chemistry of one such series of 4,4-diaryl-3,4-dihydro-1(2*H*)-phthalazinones obtained from such reactions. In the present paper, we describe the substituent effects and the structural limitations in the formation of these compounds from phthalides.

Results and Discussion

A solution of CVL (**1a**) in ethanol was heated with excess hydrazine hydrate under reflux. The reaction was conveniently monitored by TLC [silicagel, with $CHCl_3$–EtOH (5 : 1) as an eluent]; the blue spot due to the starting material (*Rf*: 0.81) was gradually replaced by the product spot (*Rf*: 0.50). The reaction went to completion in 8 hr. It was also found that the reaction was complete in 2 hr when carried out in 20% aqueous ethanolic solution. In either case, we obtained, in essentially quantitative yield, a single crystalline product (mp 266°), to which we assigned the 4,4-bis-(*p*-dimethylaminophenyl)-7-dimethylamino-3,4-dihydro-1(2*H*)-phthalazinone structure (**2a**) on the basis of its elemental analysis and spectral properties. Spectroscopic data (nuclear magnetic resonance (NMR), infrared (IR)) are presented in Table I.

3) H. Moriga and R. Oda, *Kogyo Kagaku Zasshi* (Japan), **67**, 1059 (1964), and references cited therein.

4) *a*) E.F.J. Duynstee and E. Gruncald, *J. Am. Chem. Soc.*, **81**, 4542 (1959); *b*) C.D. Ritchie, W.F. Sager, and E.S. Lewis, *ibid.*, **84**, 2349 (1962); *c*) C.D. Rithcie, G.A. Skinner, and V.G. Badding, *ibid.*, **89**, 2063 (1967); *d*) H. Nicholson and P.G. Wyatt, *J. Am. Chem. Soc.*, **92**, 5981 (1970); *e*) J.E. Doxon and T.C. Bruice, *ibid.*, **93**, 3248 (1971); *f*) C.A. Bunton and S.K. Huang, *ibid.*, **94**, 3536 (1972); *g*) D.M.E. Reuben and T.C. Bruice, *ibid.*, **98**, 114 (1976); *h*) M.L. Herz, D. Feldman, and E.M. Healy, *J. Org. Chem.*, **41**, 221 (1976).

5) For a review of photochromism in triphenylmethanes, see R.N. Macnair, *Photochemistry and Photobiology*, **6**, 779 (1967).

6) *a*) S. Kubota and T. Akita, *Yakugaku Zasshi*, **81**, 521 (1961); *b*) J. Gronoska, *Toczniki Chem.*, **39**, 245 (1965), **39**, 375 (1965).

1 2

a: $R_1=R_2=R_3=N(Me)_2$
b: $R_1=H$, $R_2=R_3=N(Me)_2$
c: $R_1=R_2=H$, $R_3=N(Me)_2$

Chart 2

Microanalytical and mass spectral data for this product established the molecular formula $C_{26}H_{31}N_5O$. The NMR spectrum of **2a** was similar to that of the starting material (**1a**) except for the presence of additional peaks (broad singlet) at δ 4.97 and 6.92 (one proton each), which were readily removed by equilibration with D_2O. The infrared spectrum of **2a** showed a strong band at 1660 cm^{-1} (NC=O), consistent with a conjugated six-membered ring lactam.[7]

A similar result, the formation of 3,4-dihydro-1(2*H*)-phthalazinone (**2**), was obtained in the case of MGL (**1b**), although the reaction conditions were considerably more severe than those required for CVL (**1a**). Heating MGL (**1b**) with excess hydrazine hydrate in 40% aqueous ethanol under reflux for *ca.* 20 hr resulted in the formation of 4,4-bis-*p*-dimethylaminophenyl-3,4-dihydro-1(2*H*)-phthalazinone (**2b**) (mp 245°) in essentially quantitative yield. The structure of **2b** follows similarly from its elemental analysis and spectral properties (see Table I).

In the case for similar formation of the corresponding 3,4-dihydro-1(2*H*)-phthalazinone (**2**) from 3-*p*-dimethylaminophenyl-3-phenylphthalide (**1c**), the reaction conditions required, if the reaction occurs at all, would be expected to be more severe than those for MGL (**1b**), in view of the above results. Indeed, it was found that the reaction was extremely slow and was not complete even upon heating **1c** with excess hydrazine hydrate in 50% aqueous ethanolic solution for a prolonged period (three days). The NMR spectrum of the reaction mixture showed it to be a 5:8 mixture of starting material (**1c**) and the product. The separation of

Table I. Spectroscopic Properties of **2**

Compound	NMR data (in $CDCl_3$, δ value)	IR data
2a	2.92 (12H, s, $N(Me)_2\times2$) 3.00 (6H, s, $N(Me)_2$) 4.97 (1H, br.s, NH) 6.92 (1H, br.s, CONH) 6.51—7.41 (11H, m, aromatic)	1660 (NC=O)
2b	2.92 (12H, s, $N(Me)_2\times2$) 4.88 (1H, br.s, NH) 7.10 (1H, br.s, CONH) 6.51—7.48 (12H, m, aromatic)	1665 (NC=O)
2c	2.90 (6H, s, $N(Me)_2$) 4.96 (1H, br.s, NH) 7.33 (1H, br.s, CONH) 6.51—7.51 (13H, m, aromatic)	1665 (NC=O)
2e	2.90 (12H, s, $N(Me)_2\times2$) 2.98 (6H, s, $N(Me)_2$) 3.16 (3H, s, N-Me) 6.51—7.11 (11H, m, aromatic)	1635 (NC=O)

7) D. Dolphin and A. Wick, "Tabulation of Infrared Spectral Data," John Wiley and Son, Inc., New York, N.Y. 1977, p. 278.

the products from the mixture was difficult by fractional recrystallization but easy by column chromatography (300 mesh silica gel, with $CHCl_3$ as an eluent). 4-(*p*-Dimethylaminophenyl)-4-(phenyl-3,4-dihydro-1(2*H*)-phthalazinone (**2c**) was isolated in 40% yield as colorless needles (mp 218°). Spectral data were in complete agreement with the assigned structure and are given in Table I. Unreacted phthalide (**1c**) was also recovered in 25% yield.

Despite several attempts under a variety of reaction conditions we have so far been unable to obtain 4,4-diphenyl-3,4-dihydro-1(2*H*)-phthalazinone (**2d**) by treating 3,3-diphenylphthalide (**1d**) with hydrazine hydrate. The pseudo first-order rate constants for dihydrophthalazinone (**2**) formation, measured in 20% aqueous ethanolic solution at 70°, are presented in Table II.

Table II. Pseudo First-order Rate Constants for the Conversion of **1** to **2**

Substrate	k, min^{-1} at 70°
1a	$2.3\pm0.2\times10^{-3}$
1b	$2.9\pm0.2\times10^{-4}$
1c	$6.4\pm0.4\times10^{-6}$
1d	0

It is clear, from the above results, that the introduction of dimethylamino substituents at the *para* position on the benzene ring is necessary for the formation of such 3,4-dihydro-1(2*H*)-phthalazinones (**2**). In view of the electron-donating nature of dimethylamino substituents the rate of formation of the dihydrophthalazinone (**2**) presumably decreases as the ability of the substituent to stabilize the carbocation decreases. Thus, the reaction would appear to proceed *via* a carbonium intermediate even in rather strongly basic media.

We have also carried out similar reactions of CVL (**1a**) with various substituted hydrazines other than hydrazine hydrate. Among these, only methylhydrazine yielded the corresponding 2-methyl-3,4-dihydrophthalazinone (**2e**) (mp 213°), but in rather poor yield (34%). The structure of **2e** follows from its spectroscopic properties (Table I) and an independent synthesis by methylation of **2a**. This result is rather unexpected, in the light of the mechanism described above, since the nucleophilic attack of alkylated hydrazine usually occurs through the substituted nitrogen. This could be ascribed to steric crowding on the carbocation center due to the presence of the two aryl groups.

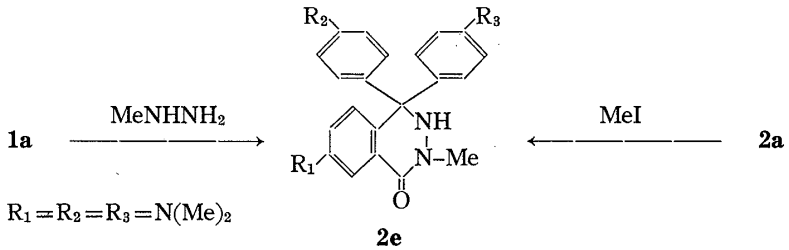


Chart 3

To further assess the influence of structural change on the formation of dihydrophthalazinone, N,N,N′,N′-tetramethyl rhodamine (**3**)[8] was allowed to react with hydrazine hydrate. The reaction was very rapid ($k=3.0\times10^{-2}$ min^{-1} at 70°) and the product was the N-aminophthalimidine derivative (**4**) in nearly quantitative yield. The structure of **4** was further substantiated by its conversion to the N-isopropylideneamino derivative (**5**).

This result seems to be of interest. Steric interactions between the 1,8-protons of the coplanar xanthyl array and *o*-protons of the 9-aryl ring force the carbonium intermediate

8) D.R.P. Bindschedler, *Frdl.*, **4**, 261 (1894).

to adopt a conformation perpendicular to the xanthyl plane. The acceleration of the reaction rate, therefore, could arise from a greater contribution of the dimethylamino substituent effect due to the coplanarity of the xanthyl array and a reduced contribution of the *o*-substituent (carboxyl function) effect of the 9-aryl ring due to the above orthoganality. Attack of hydrazine to the carbonium intermediate would result in the formation of (3′), in which the rotation about the nitrogen-carbon bond of the hydrazino group is severely sterically hindered due to the 9-aryl ring; it may be forced to take an eclipse-like conformation. The subsequent ring closure, therefore, could occur at the site of the nitrogen to give the N-aminophthalimidine (**4**) exclusively.

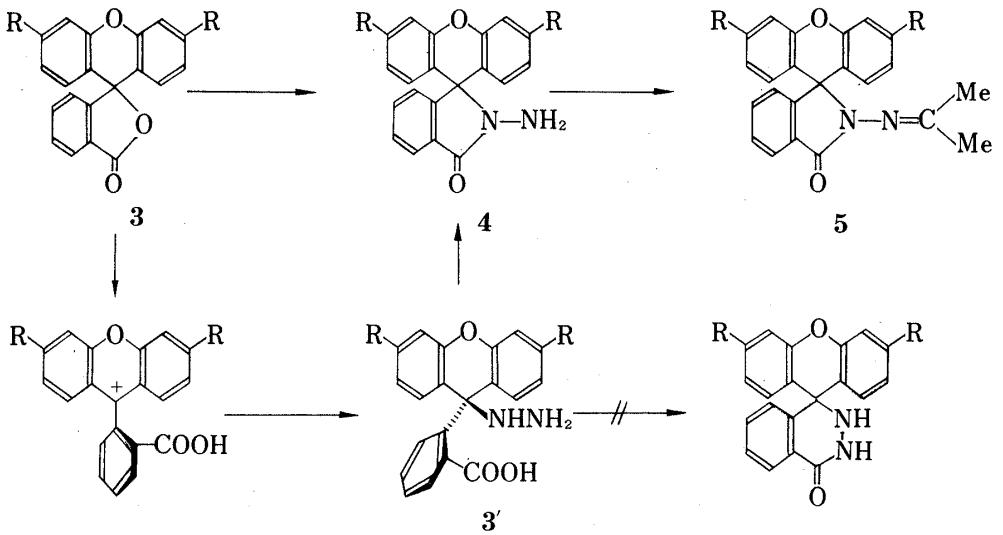


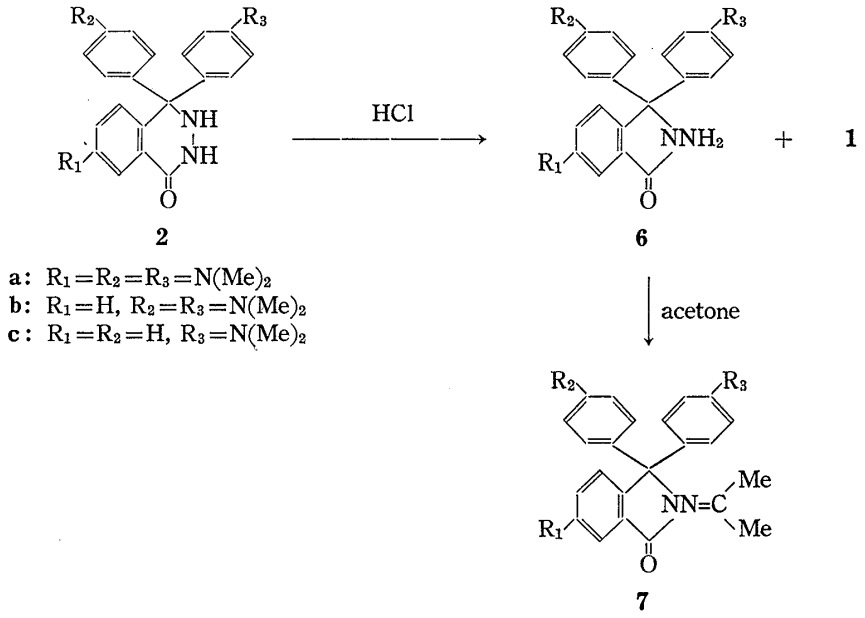
Chart 4

Although the dye cations of crystal violet and malachite green can be placed in the class of the most stable carbocations,[9] the attack of nucleophiles such as hydrazines is known to be still rapid,[3f] and the same would be true in the case of the compounds (**1**), since the solutions never display any color [due to (I)], during the course of the reaction. The great facility with which hydrazine reacts with the carbocations (I) is confirmed by the observation that a hot aqueous ethanolic solution containing CVL (**1a**), which exhibits a blue color, reacts with hydrazine instantaneously on mixing, as determined by discharge of the blue color.

With a view to examining some chemical properties of these compounds (**2a**—**c**), several experiments were carried out. The compounds (**2a**—**c**) were heated in *ca.* 18% hydrochloric acid for 2 hr, as reported by Kubota,[6a] to result in smooth conversion into two products in each case. Chromatographic separation gave the corresponding N-aminophthalimidines (**6a**—**c**) as the major product, in addition to the phthalides (**1a**—**c**), which were identified by comparison with authentic samples (mp, NMR, IR). The yield ratios were rather variable, as shown in Chart 5. The structures of **6a**—**c** were established on the basis of their elemental analysis data and spectral properties. Spectroscopic data (NMR, IR) are given in Table III. Further confirmation of the N-aminophthalimidine structure was provided by their facile conversion to the corresponding N-isopropylidenamino-phthalimidines (**7a**—**c**) when heated in acetone in the presence of trace amounts of acetic acid, as shown in Chart 5.

Thus, one possible scheme which accounts for these ring contractions is shown in Chart 6, using **2b** as an example. In strongly acidic media (used in the above reaction), **2b** undergoes

9) For a review of triaryl carbocations, see H.H. Freedman, in "Carbonium Ions," Vol. IV, G.A. Olah and P.V. Schleyer, Ed., Wiley-Interscience, New York, N.Y. 1972. p. 1501.



2

a: $R_1=R_2=R_3=N(Me)_2$
b: $R_1=H$, $R_2=R_3=N(Me)_2$
c: $R_1=R_2=H$, $R_3=N(Me)_2$

6

7

Chart 5

TABLE III. Spectroscopic Properties of **6**

Compound	NMR data (in $CDCl_3$, δ value)	IR data
6a	2.92 (12H, s, $N(Me)_2\times2$) 2.99 (6H, s, $N(Me)_2$) 3.86 (2H, br.s, NH_2) 6.51—7.21 (11H, m, aromatic)	3400 (br. NH_2) 1680 (NC=O)
6b	2.96 (12H, s, $N(Me)_2\times2$) 3.60 (2H, br.s, NH_2) 6.52—7.45 (12H, m, aromatic)	3400 (br. NH_2) 1690 (NC=O)
6c	2.99 (6H, s, $N(Me)_2$) 3.65 (2H, br.s, NH_2) 6.51—7.55 (13H, m, aromatic)	3400 (br. NH_2) 1685 (NC=O)

heterolytic cleavage of the 3,4-dihydrophthalazinone ring and subsequently produces the multi-cation. Thus, the protonated dimethylamino substituent would have a destabilizing inductive effect on the triphenyl carbocation, which would appear to be the driving force for this conversion, *i.e.*, the reorganization of the destabilized carbocation with either N or O of the amido functional moiety on the hydrazide group to give the product (**6**) and MGL (**1b**) after hydrolysis.

When chloroform–ethanol (1: 1) solution containing compound (**2a**) was treated with a weak acid such as dilute hydrochloric acid or bentonite, **2a** does in fact instantaneously exhibit a greenish-blue color, but not as intensely as CVL (**1a**) does, indicating that **2a** also undergoes heterolytic cleavage of the 3,4-dihydrophthalazinone ring to form the corresponding triphenyl methane cation dye on exposure to an electrophilic reagent. However, perhaps the most remarkable features of **2a** are that, unlike CVL, it shows exceptional sensitivity to ultraviolet light, and also, that compound (**2a**) and (**2b**) were found to be excellent initiators of photo-polymerization for unsaturated compounds.[10]

10) The tests of **2a** as an additive for photo-polymerization were performed by Wako Pure Chemical Industries. Ltd. (Osaka, Japan), and their help is gratefully acknowledged. Details of the studies on these photolytic properties will be reported elsewhere.

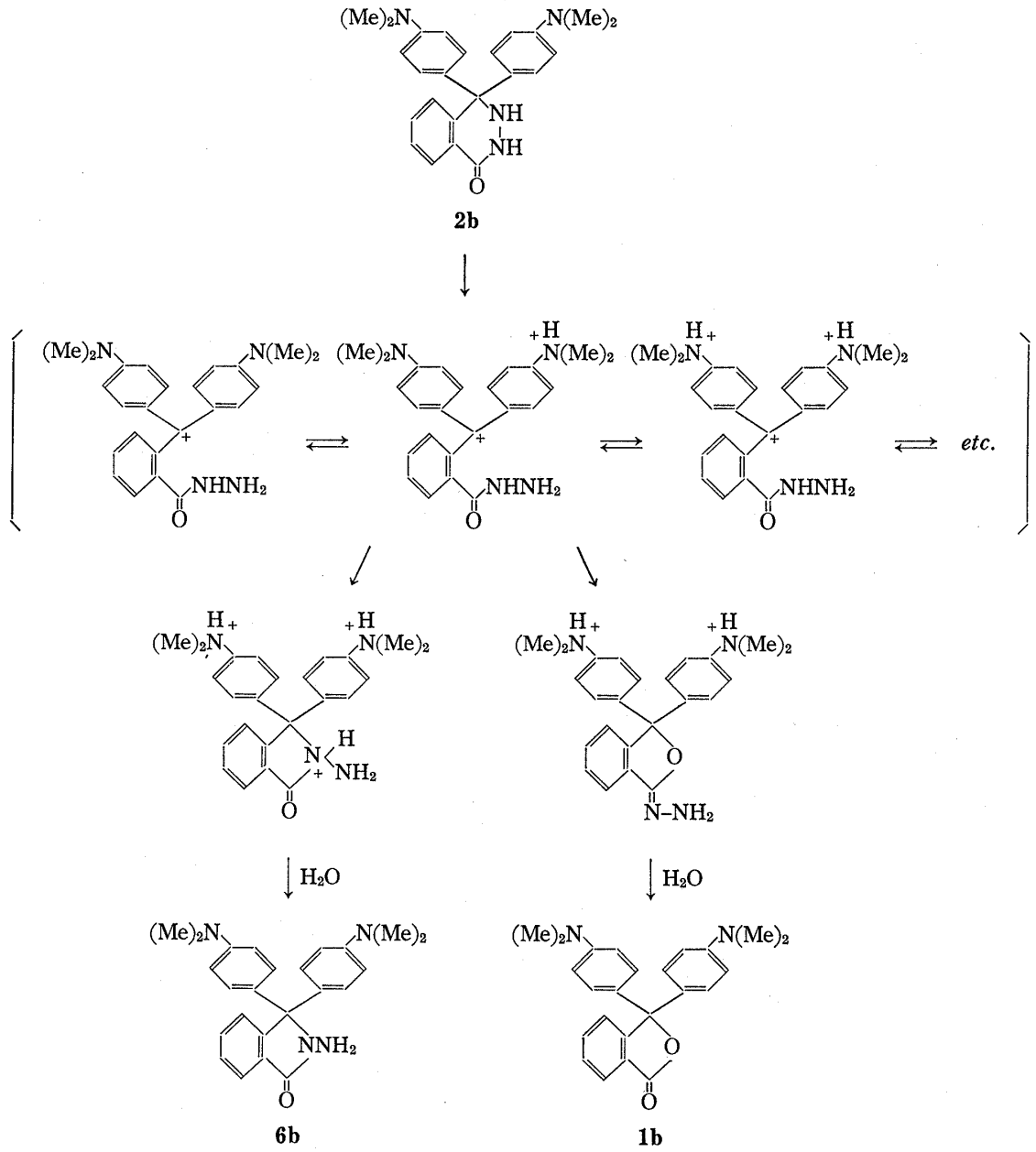


Chart 6

In conclusion, it became obvious from our results reported herein not only that the direct formation of **2** from 3,3-diarylphthalide required a powerful electron-donating substituent to facilitate the lactone-ring opening by stabilizing the carbocation formed, (indicating that a less direct route should be devised for the preparation of **2** bearing an electron-withdrawing substituent on the 4,4-diaryl groups), but also that replacement of the 3,3-diaryl groups on the phthalide by the xanthyl group or probably any other coplanar substituent completely changed the product formed. Further studies on the chemistry and reactions, including photochemical behavior, of **2** are in progress.

Experimental

NMR spectra were obtained on a Hitachi R-20 spectrometer (60 MHz), in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. All chemical shifts are in parts per million (δ) from TMS. IR spectra were taken as KBr discs with a JASCO IRA-T spectrophotometer and were calibrated against polystyrene. UV spectra were measured in 95% ethanol with a Hitachi 323 spectrophotometer. Mass spectra were obtained

at 70 eV with a JEOL JMS-D300 spectrometer. A Du Pont 840 liquid chromatograph equipped with an ultraviolet absorption detector (254 nm) and a high pressure pump was used for the determination of the conversion for kinetic measurements.[11] Elemental analyses were carried out by the Microanalytical Laboratory, Gifu College of Pharmacy. All melting points are uncorrected.

4,4-Bis-(*p*-dimethylaminophenyl)-7-dimethylamino-3,4-dihydro-1(2*H*)-phthalazinone (2a)——(A) A solution of CVL (**1a**) (4.15 g) and 100% hydrazine hydrate (5.0 g) in ethanol (200 ml) was heated under reflux for 8 hr. The reaction mixture was concentrated to about half the initial volume under reduced pressure and cooled. The precipitated solid was collected and recrystallized from ethanol to give (**2a**) (3.5 g) as pale yellow needles, mp 266°. *Anal.* Calcd for $C_{26}H_{31}N_5O$: C, 72.68; H, 7.29; N, 16.30. Found: C, 72.70; H, 7.30; N, 16.18. UV λ_{max} nm (ε) 266 (57000), MS *m/e*: 429 (M^+). For NMR and IR spectra, see Table I.

(B) A solution of CVL (**1a**) (4.15 g) and 100% hydrazine hydrate (5.0 g) in 20% aqueous ethanol (200 ml) was heated under reflux for 2 hr. The reaction mixture was then worked up as above to give (**2a**) (3.7 g) as pale yellow needles; this material was identical (NMR, IR) with (**2a**) obtained by method (A).

4,4-Bis-(*p*-Dimethylaminophenyl)-3,4-dihydro-1(2*H*)-phthalazinone (2b)——A solution of MGL (**1b**) (1.86 g) in 40% aqueous ethanol was heated with 100% hydrazine hydrate (2.5 g) under reflux for 20 hr, then cooled. The precipitated solid was collected, washed with water and recrystallized from ethanol to give (**2b**) (1.50 g) as colorless needles, mp 245°. *Anal.* Calcd for $C_{24}H_{26}N_4O$: C, 74.57; H, 6.79; N, 14.50. Found: C, 74.87; H, 6.80; N, 14.70. UV λ_{max} nm (ε) 254 (46000). MS *m/e*: 386 (M^+). For NMR and IR spectra, see Table I.

4-*p*-Dimethylaminophenyl-4-phenyl-3,4-dihydro-1(2*H*)-phthalazinone (2c)——A solution of **1c** (1.65 g) in 50% aqueous ethanol was heated with 100% hydrazine hydrate (2.5 g) under reflux for 72 hr. The reaction mixture was concentrated to about half the initial volume, and chloroform was added. The chloroform solution was washed with ether and dried over anhydrous sodium sulfate. The crude mixture obtained by removal of the chloroform under reduced pressure was chromatographed on 300 mesh silica gel with chloroform as an eluent to give **1c** (0.40 g), which was identical with an authentic sample, and **2c** (0.70 g) as colorless needles, mp 218°. *Anal.* Calcd for $C_{22}H_{21}N_3O$: C, 76.79; H, 6.16; N, 12.24. Found: C, 76.77; H, 6.30; N, 12.08. UV λ_{max} nm (ε) 263 (20000). MS *m/e*: 343 (M^+). For NMR and IR spectra, see Table I.

2-Methyl-4,4-bis-(*p*-dimethylaminophenyl)-7-dimethylamino-3,4-dihydrophthalazinone (2e)——(A) A solution of **1a** (4.15 g) in 20% aqueous ethanol (150 ml) was heated with methylhydrazine (5.6 g) under reflux for 10 hr. After removal of the solvent under reduced pressure, the viscous residue was taken up in chloroform. The chloroform solution was washed with water and dried over anhydrous sodium sulfate. The crude mixture obtained by removal of the solvent was chromatographed on 300 mesh silica gel ($CHCl_3$ eluent) to give **1a** (0.8 g) in the first fraction and **2e** (1.5 g) in the second fraction as colorless needles (EtOH), mp 213°. *Anal.* Calcd for $C_{27}H_{33}N_5O$: C, 73.11; H, 7.50; N, 15.79. Found: C, 72.95; H, 7.37; N, 15.59. UV λ_{max} (ε) 267 (27500). MS *m/e*: 443 (M^+). For NMR and IR spectra, see Table I.

(B) A solution of **2a** (4.30 g) in DMF (30 ml) was stirred with methyliodide (4.23 g) in the presence of anhydrous potassium carbonate (4.14 g) at room temperature overnight. Excess potassium carbonate was removed by decantation, then the reaction mixture was concentrated to dryness. The residue was taken up in chloroform. The chloroform solution was washed with water and dried over anhydrous sodium sulfate. The crude mixture obtained by concentration was chromatographed on silica gel to give **2e** (0.45 g) as the third fraction; this product was identical (NMR, IR) with that obtained by method (A).

Spiro[3,6-bis-(*p*-dimethylamino)-xanthene-9,3′-N-aminophthalimidine] (4)——A solution containing **3** (2.0 g) and hydrazine hydrate (2.7 g) in ethanol (60 ml) was allowed to stand at room temperature for 5 hr. The reaction mixture was concentrated almost to dryness under reduced pressure. The residue was taken up in chloroform. The chloroform solution was washed with water, and dried over anhydrous sodium sulfate. The crude mixture obtained by removal of the solvent was recrystallized from ethanol to give **4** (1.8 g) as almost colorless needles, mp 245° (dec.). *Anal.* Calcd for $C_{24}H_{24}N_4O_2$: C, 71.98; H, 6.04; N, 13.99. Found: C, 72.20; H, 6.06; N, 13.98. UV λ_{max} nm (ε): 238 (61100), 268 (32500), 306 (12200). IR cm^{-1}: $\nu_{C=O}$ 1670: MS *m/e*: 400 (M^+). NMR ($CDCl_3$) δ: 2.93 (12H, N-methyl), 3.62 (2H, NH_2), 6.34 (2H, d.d, $J=2.3$ and 8.3 Hz, H_2 and H7), 6.47 (2H, d, $J=2.3$ Hz, H_4 and H_5), 6.49 (2H, d, $J=8.3$ Hz, H_1 and H_8), 6.94—7.48 and 7.78—8.00 (4H, m, aromatic).

3,3-Bis-(*p*-dimethylaminophenyl)-6-dimethylamino-N-aminophthalimidine (6a)——A solution of **2a** (1.29 g) in *ca.* 18% hydrochloric acid (20 ml) was heated under reflux for 2 hr. After cooling, the reaction mixture was diluted with water and neutralized with 20% sodium hydroxide solution with ice cooling, then extracted with chloroform. The chloroform layer, combined with washings, was then washed with water and dried over anhydrous sodium sulfate. An NMR spectrum of the residue obtained by removal of the chloroform under reduced pressure showed it to be a *ca.* 1:2 mixture of CVL (**1a**) and **6a**. The crude mixture was then separated by a column chromatography (300 mesh silica gel) with chloroform as an eluent to give CVL (**1a**) (0.33 g), which was identical with an authentic sample in every respect, and **6a** (0.70 g), which was

11) We are grateful to Dr. T. Hayashi for running HPLC and obtaining the chromatogram. For details of the assembled apparatus, see T. Hayashi, T. Sugiura, S. Kawai, and T. Ohno, *J. Chromatogr.*, **1978**, 141.

further purified by recrystallization from ethanol to give colorless needles, mp 230°. *Anal.* Calcd for $C_{26}H_{31}N_5O$: C, 72.70; H, 7.27; N, 16.30. Found: C, 72.73; H, 7.43; N, 16.08. For NMR and IR spectra, see Table III.

3,3-Bis-(*p*-dimethylaminophenyl-N-aminophthalimidine (6b)——A solution of **2b** (1.16 g) in *ca.* 18% hydrochloric acid (20 ml) was heated under reflux for 2 hr. The reaction mixture was then worked up as above to give MGL (**1b**) (0.40 g), which was identical with an authentic sample, and **3b** (0.71 g) as pale green crystals, mp 89—92°. Further purification by recrystallization was rather difficult. MS *m/e*: 386 (M^+). For NMR and IR data, see Table III.

3-*p*-Dimethylaminophenyl-3-phenyl-N-aminophthalimidine (6c)——A solution of **2c** (1.50 g) in *ca.* 18% hydrochloric acid (20 ml) was heated under reflux for 2 hr. The reaction mixture was then worked up as in the case of **2a** to give **1c** (0.22 g), which was identical with an authentic sample, and **3c** (0.84 g) as pale yellow crystal, mp 102—104°. Further purification by recrystallization was rather difficult. MS *m/e*: 343 (M^+). For NMR and IR spectra, see Table III.

Spiro[3,6-bis-(*p*-dimethylamino)-xanthene-9,3′-N-isopropylideneamino-phthalimidine (5)——A solution of **4** (0.20 g) in acetone (25 ml) and trace amounts of acetic acid was heated under reflux for 5 hr. The reaction mixture was concentrated to dryness under reduced pressure. The residue was taken up in chloroform. The chloroform solution was washed with water and dried over anhydrous sodium sulfate. The residue obtained by removing the chloroform was recrystallized from ethanol to give **5** (0.18 g) as almost colorless crystals, mp 237° (dec.). *Anal.* Calcd for $C_{27}H_{28}N_4O_2$: C, 73.61; H, 6.41; N, 12.72. Found: C, 73.40; H, 6.49; N, 12.47. UV λ_{max} nm (ε): 239 (56700), 270 (44700), 313 (12200). MS *m/e*: 440 (M^+). NMR ($CDCl_3$) δ: 1.78 and 1.91 (3H×2, allylic methyl), 2.90 (12H, N-methyl), 6.32 (2H, d.d, J=2.3 and 8.3 Hz, H_2 and H_7), 6.42 (2H, d, J=2.3 Hz, H_4 and H_5), 6.56 (2H, d, J=8.3 Hz, H_1 and H_8), 6.97—7.56 and 7.81—9.97 (4H, m, aromatic).

3,3-Bis-(*p*-dimethylaminophenyl)-6-dimethylamino-N-isopropylideneamino-phthalimidine (7a)——A solution of **6a** (0.50 g) in acetone (20 ml) with a trace amount of acetic acid was heated under reflux for 6 hr. On cooling, greenish-yellow crystals precipitated. These were collected, washed with water and recrystallized from ethanol to give **7a** (0.35 g) as pale yellow needles, mp 248—250°. *Anal.* Calcd for $C_{29}H_{35}N_5O$: C, 74.17; H, 7.51; N, 14.19. Found: C, 74.13; H, 7.32; N, 14.19. UV λ_{max} nm (ε): 270 (32500). IR cm^{-1}: $\nu_{C=O}$ 1680. MS *m/e*: 469 (M^+). NMR ($CDCl_3$) δ: 1.48 and 2.05 (3H×2, allylic methyl), 2.90 (12H, N-methyl), 2.98 (6H, N-methyl), 6.57—7.25 (11H, m, aromatic).

3,3-Bis-(*p*-dimethylaminophenyl)-N-isopropylideneamino-phthalimidine (7b)——A solution of **6b** (0.50 g) in acetone (20 ml) with a trace amount of acetic acid was heated under reflux for 6 hr. The reaction mixture was concentrated to dryness under reduced pressure. The residue was taken up in chloroform. The chloroform solution was washed with water and dried over anhydrous sodium sulfate, then the residue obtained by removing the chloroform under reduced pressure was recrystallized from ethanol to give **7b** (0.26 g) as pale green needles, mp 214°. *Anal.* Calcd for $C_{27}H_{30}N_4O$: C, 76.03; H, 7.09; N, 13.13. Found: C, 75.88; H, 7.17; N, 12.79. UV λ_{max} nm (ε): 269 (28800). IR cm^{-1}: $\nu_{C=O}$ 1670, MS *m/e*: 420 (M^+), NMR ($CDCl_3$) δ: 1.50 and 2.04 (3H×2, allylic methyl), 2.86 (12H, N-methyl), 6.51—7.38 (12H, m, aromatic).

3-*p*-Dimethylamino-3-phenyl-N-isopropylideneamino-phthalimidine (7c)——A solution of **6c** (0.50 g) in acetone (20 ml) with a trace amount of acetic acid was heated under reflux for 6 hr. The reaction mixture was then worked up as in the case of **6b** to give **7c** (0.47 g) as a solid mass. Purification by recrystallization failed. IR cm^{-1}: $\nu_{C=O}$ 1685. MS *m/e*: 371 (M^+). NMR ($CDCl_3$) δ: 1.46 and 2.05 (3H×2, allylic methyl), 2.83 (6H, N-methyl), 6.51—7.41 (13H, m, aromatic).

Kinetics——The technique used for the rate measurements was to prepare a 20% aqueous ethanolic solution (80 ml) containing 0.3 mmol of the reactant and a similar solution (20 ml) containing 20 mmol of 100% hydrazine hydrate. The two solutions were placed in a thermostated bath at 70°, then mixed and kept in the bath at 70°. Aliquots (1 ml) were withdrawn periodically by means of a syringe and diluted to 30 ml in the case of CVL (**1a**), and to 20 ml in the case of MGL (**1b**) and **1c** with cold 20% aqueous ethanol. 60 μl of the resulting solution was then subjected to HPLC (200×2.1 mm column of Lichrosorb RP-18 (5 μm); flow rate 0.6 ml/min), at 50°, with 60—95% aqueous acetonitrile gradient elution. The peak height ratio of the starting reactant (**1**) and the product (**2**) was determined and the conversion of the reaction was read off from a calibration graph previously obtained from the peak heights of authentic samples of **1** and **2**. The pseudo first-order rate constants are averages of at least four runs in each case and are given in Table II.