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The Synthesis of Monosubstituted Derivatives of 6-Amino-3,3′-bis(*p*-dimethylaminophenyl)phthalide

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ABSTRACT

A practicable method for the nitration of Malachite Green lactone at carbon atom C-6 yielding 3,3′-bis(dimethylaminophenyl)-6-nitrophthalide is presented. Reduction furnished the corresponding C-6 aminophthalide which served as starting material for a series of various N*-monosubstituted derivatives. The amino group was also used to synthesize pyrroles, and via the corresponding azide, triazole and phosphazo derivatives.*

1 INTRODUCTION

The acid-induced ring cleavage of originally colorless lactone systems as precursors to yield colored carbonium ions became of considerable commercial importance in imaging systems. The best-known examples are represented by Crystal Violet lactone and related compounds, of which the latter may be considered as having the structural moiety of Crystal Violet lactone built inherently into their carbon framework.

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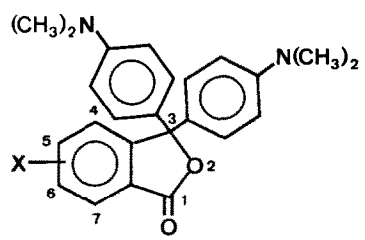
Crystal Violet lactone and Malachite Green lactone are derivatives of 3,3′-disubstituted phthalide structures which display with acidic reagents (co-reactants) intense blue and blue–green colors, respectively.

Little attention has been paid to synthetic variations with respect to various substituents attached to the C-6 carbon atom of the phthalide ring, and the impact those substituents may exert on the color image of the carbonium ion.

Theoretical considerations led us to construct a conceptual framework within which the experiments could be conceived and then to construct a pertinent interface with the color images.

The nitration of 3,3′-bis(4-dimethylaminophenyl)phthalide (**1**), generally referred to as Malachite Green lactone, was believed to yield, according to a patent disclosure,[1] the C-5 nitro isomer **2**. However, some years later the assumed structure was duly revised,[2] and was now correctly assigned to that having the nitro group positioned at the carbon atom C-6 (**3**). This was deduced from the calculated chemical shifts for the protons of the phthalide fragment and compared with the experimental values obtained for the related Crystal Violet lactone (**4**). Additional experimental evidence arose from the transformation of the nitro to a dimethylamino group, thus supporting the NMR data.

The 6-nitrophthalide derivative (**3**) was also mentioned in a patent,[3] although without specifying any of the characteristic details such as physical constants or the method of preparation.



1 X = H

2 X = 5-NO_2

3 X = 6-NO_2

4 X = 6-$N(CH_3)_2$

5 X = 6-NH_2

The nitration of Malachite Green lactone would offer a feasible route and an amenable access to derivatives of the phthalide system having various substituents attached to the C-6 carbon atom. By far the most important and also the best-known representative is the C-6 dimethylamino derivative,

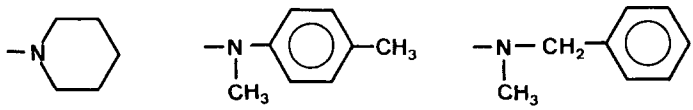


Fig. 1.

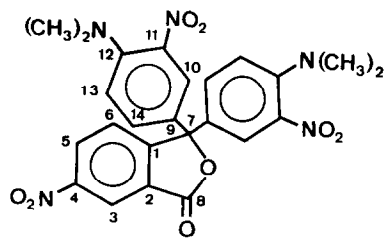
better known as Crystal Violet lactone (**4**), which is commercially used as a color-former in imaging systems.[4]

Considerably less knowledge, however, has been assembled concerning the synthesis and color-forming properties of 3,3'-disubstituted phthalide systems in which various substituents are attached to the phthalide moiety, and which, having an electronic influence different from the dimethylamino group, contribute to the facile shift from a colorless state to that of a very intense color, e.g. the formation of a triphenylmethylcarbonium ion.

The synthesis of the few known structural types relied on the ease of accessibility of a readily amenable precursor such as *N*-mono- or di-substituted *m*-aminobenzoic acids. They provided one of the building blocks which then furnished the phthalide moiety of the molecule, as has been exemplified in the synthesis of derivatives displaying structural units such as those shown in Fig. 1, attached to the carbon atom C-6.[5]

2 RESULTS AND DISCUSSION

The method of preparation and the yield of Malachite Green lactone have been considerably improved,[6] and this led us to repeat the reported nitration of **1** according to the specification given in the patent cited above.[1] However, we obtained consistently mixtures which contained only 50–60% of **3**. The accompanying products were identified as the trinitro derivative **6** and 2–4% of starting material.



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Small quantities of pure **3** could only be obtained from this mixture by chromatographic purification on silica gel. The compound was isolated as orange crystals having a melting point of 168–169°C as reported in the literature.[1]

TABLE 1
C-6 Substituted 3,3′-bis(*p*-dimethylaminophenyl)phthalides

Compound no.	*R*	*M.p. (°C) (solvent)*	*Yield (%)*	*Formula*	*Analysis (%) Calcd./Found*						
					C	*H*	*N*	*F*	*S*	*Si*	*P*
7	NH—CHO	124–126 (CH_3OH)	83	$C_{25}H_{25}N_3O_3$	72·3 72·2	6·1 6·2	10·1 9·8				
8	NH—CO—CH_3	114–116[a]	89	$C_{26}H_{27}N_3O_3$	72·7 72·5	6·3 6·5	9·8 10·1				
9	NH—CO—C_2H_5	132–134 (C_7H_8/CH_3CN, 11:1)	58	$C_{27}H_{29}N_3O_3$	73·1 73·2	6·6 6·7	9·5 9·3				
10	NH—CO—$C(CH_3)_3$	230–232 (CH_3CN)	100	$C_{29}H_{33}N_3O_3$	73·9 73·8	7·1 7·1	8·9 9·1				
11	NH—CO—CH=CH—C_6H_5	108–110 (C_7H_8/CH_3CN, 9:1)	77	$C_{33}H_{31}N_3O_3$	76·6 76·7	6·1 6·1	8·1 7·9				
12	NH—CO—C_6H_5	222–223 (C_7H_8/CH_3CN, 10:1)	100	$C_{31}H_{29}N_3O_3$	75·7 75·9	6·0 6·1	8·6 8·2				
13	NH—CO—C_6H_4—OCH_3(*p*)	123–124 (C_7H_8/CH_3CN, 5:1)	96	$C_{32}H_{31}N_3O_4$	73·7 73·7	6·0 6·1	8·1 8·0				
14	NH—CO—C_6H_4—CF_3(*p*)	178–180 (C_7H_8/CH_3CN, 9:1)	87	$C_{32}H_{28}F_3N_3O_3$	68·7 68·6	5·0 5·0	7·5 7·5	10·2 10·1			
15	NH—CO—C_6H_2(3,4,5-OCH_3)$_3$	204–206 (C_7H_8/CH_3CN, 12:1)	84	$C_{34}H_{35}N_3O_6$	70·2 70·2	6·1 6·2	7·2 7·1				
16	NH—CO—2-thiophenyl	118–119 (C_7H_8/CH_3CN, 9:1)	66	$C_{29}H_{27}N_3O_3S$	70·0 70·1	5·5 5·4	8·4 8·4		6·4 6·5		
17	NH—SO_2—CH_3	117–120[a]	50	$C_{25}H_{27}N_3O_4S$	64·5 64·6	5·8 6·0	9·0 9·1		6·9 6·7		

18	NH—SO_2—C_6H_4—CH_3(*p*)	134–135 (CH_3CN)	62	$C_{31}H_{31}N_3O_4S$	68·8 69·0	5·8 5·8	7·8 8·0	5·9 5·8		
19	NH—CO—$N(CH_3)_2$	152–154[a] (C_7H_8/CH_3CN, 9:1)	37	$C_{27}H_{30}N_4O_3$	70·7 71·0	6·6 6·5	12·2 12·0			
20	NH—CO—NH—C_2H_5	140–145[a] (C_7H_8/CH_3CN, 9:1)	43	$C_{27}H_{30}N_4O_3$	70·7 71·0	6·6 6·6	12·2 12·1			
21	NH—P(O)$(OCH_3)_2$	228–229 (C_7H_8/CH_3CN, 1:1)	55	$C_{26}H_{30}N_3O_5P$	63·0 63·3	6·1 6·2	8·5 8·5			6·3 6·2
22	NH—$Si(CH_3)_2C(CH_3)_3$	170–173[a]	60	$C_{30}H_{39}N_2O_2Si$	71·8 71·6	7·8 7·9	8·4 8·3		5·6 5·5	
23	NH—$(CH_2)_2$—CN	95–97[a] (C_7H_8)	8	$C_{27}H_{28}N_4O_2$	73·6 73·8	6·4 6·5	12·7 12·6			
24	NH—$(CH_2)_2$—$COOCH_3$	78–79 (C_7H_8)	63	$C_{28}H_{31}N_3O_4$	71·0 70·9	6·6 6·8	8·9 8·9			
25	1-pyrrolyl	210–213 (CH_3CN)	89	$C_{28}H_{27}N_3O_2$	76·9 77·0	6·2 6·3	9·6 9·5			
26	2,5-$(CH_3)_2$—1-pyrrolyl	136–138 (CH_3CN)	71	$C_{30}H_{31}N_3O_2$	77·4 77·5	6·7 6·7	9·0 9·1			
27	N_3	185 (C_7H_8/CH_3CN, 1:1)	91	$C_{24}H_{23}N_5O_2$	69·7 69·6	5·6 5·7	16·9 17·1			
28	4,5-$(CH_3OOC)_2$—1,2,3-triazol-1-yl	191 (C_7H_8)	61	$C_{30}H_{29}N_5O_6$	64·9 65·0	5·3 5·3	12·6 12·7			
29	N=P$(C_6H_5)_3$	231–233 (C_7H_8)	43	$C_{42}H_{38}N_3O_2P$	77·9 77·7	5·9 5·9	6·5 6·6			4·8 4·8
30	N=N—N=P$[(CH_3)_2N]_3$	186 (C_7H_8/CH_3CN, 1:1)	57	$C_{30}H_{41}N_6O_2P$	62·5 62·5	7·2 7·2	19·4 19·2			5·4 5·5
31	N(CH_3)—SO_2—C_6H_4—CH_3(*p*)	177 (CH_3CN)	90	$C_{32}H_{33}N_3O_4S$	69·2 69·0	6·0 6·1	7·6 7·8	5·8 5·7		

[a] Purified by chromatography on silica gel.

Attempts to prepare large quantities of **3** merely by crystallization of the crude nitrated mixture were unsuccessful.

The trinitro derivative **6** was prepared separately by nitration of **1** at 35–40°C in sulfuric acid as solvent. Its structure was ascertained by its infrared and NMR spectral data as well as the analytical results.

However, the slow addition of 1·43 mol of fuming nitric acid (100%), which had been carefully freed of all nitrous oxides before use,[7] to a solution of 1 mol of **1** in concentrated sulfuric acid met with success. There was only a small temperature interval (16–18°C) where the reaction proceeded at a satisfactory rate, thus simultaneously avoiding formation of sizable quantities of the unwanted trinitro derivative **6**. This procedure furnished product mixtures containing 83–92% of the 6-nitro derivative **3** apart from 2·6–7% of **1** and varying amounts of **6**, generally less than 2%. The total yields of products ranged from 93 to 98% based on **3**. Extended reaction times and an increase of temperature notably favored the formation of **6**.

The rather large volume of concentrated sulfuric acid used in the patented reaction process[1] could be substantially reduced, e.g. from 16·7 ml g^{-1} to 2·8 ml g^{-1}.

Since the synthetic target was centered on a practical synthesis of 6-aminophthalide (**5**) the crude mixture obtained in the nitration reaction was subjected to catalytic hydrogenation. Subsequent work-up removed all adherent impurities and furnished pure aminophthalide (**5**).[1,2] The physical properties of **5** were in agreement with the data reported in the literature.[1,2] It has been mentioned in a patent[8] that methyleneimino fragments attached to the C-6 carbon atom of the phthalide ring (e.g. Schiff bases of **5**) imparted a green or a blue–green color on paper in contact with a co-reactant. Having an entirely practical and expedient procedure for **3** at hand, we deemed it of interest to connect with the nitrogen atom structural functionalities involving π-systems such as the formyl group, variously substituted keto groups, sulfones, ureas and phosphorus esters, or to build the nitrogen atom into a heterocyclic ring system. The synthesis of these derivatives (**7**–**21**) followed known synthetic schemes and their physical data are compiled in Table 1.

The synthesis of *N*-substituted pyrroles was achieved by reacting the amine **5** with either 2,5-dimethoxydihydrofuran or with acetonylacetone yielding **25** and **26**, respectively.

Diazotization of **5** and subsequent reaction of the diazonium azide yielded the 6-azidophthalide (**27**) from which the phosphoranes (**29**, **30**) were prepared. The reaction of **27** with tris(dimethylamino)phosphine provided a noteworthy exception, in that no evolution of nitrogen occurred, but rather the formation of stable triazaphosphazene (**30**) was observed. The structure was confirmed by the ^{14}N-NMR spectra. This represents one of the very few

examples in which the intermediate phosphazene having three linearly arranged nitrogen atoms proved to be a stable compound in the course of the Staudinger reaction.[9] Furthermore, the azide gave rise to a 1,2,3-triazole (**28**) on reaction with dimethyl acetylenedicarboxylate.

These compounds, in contact with a co-reactant such as activated clay, displayed a bright green color, some of them exhibiting a remarkable light stability, comparable with or even better than that of Crystal Violet lactone. However, a π-electron system may also be built into a heterocyclic moiety such as **25**, **26** or **28**, so as to produce a new absorption band which essentially causes the compounds to display a green image. The phosphoranes also imparted a green color on clay which, however, faded soon after being exposed to daylight.

Subsequent methylation of the monosubstituted amine (**18**) was readily achieved using dimethyl methylphosphonate as the methylating agent,[10,11] yielding **31**.

Comparison of the color-forming properties of **18** and **31** clearly showed that disubstitution shifted the absorption maximum to shorter wavelength, e.g. the latter compound imparted a blue color again on clay.Three examples (**22–24**) showed that monosubstitution of the amine **5** by a moiety bearing a carbon or silicon atom but being deficient of a π-system, displayed on clay again the usual blue color similar to that observed with **4** or with **5**.

3 EXPERIMENTAL

Materials and methods

Melting points were determined in open capillary tubes and are uncorrected. Samples for the infrared spectra were prepared in potassium bromide pellets. 3,3'-Bis (*p*-dimethylaminophenyl)phthalide (Malachite Green lactone) was prepared according to the literature.[6]

Bis(*p*-dimethylaminophenyl)-6-nitrophthalide (3)

To 34 ml of concentrated sulfuric acid were added 12 g (0·032 mol) of 3,3'-bis(dimethylaminophenyl)phthalide. The suspension was stirred and heated to 50°C until all the crystals had dissolved. Then the solution was cooled to 14–15°C and a solution of 4·6 ml (0·046 mol) of colorless nitric acid[7] (100%) dissolved in 10 ml of concentrated sulfuric acid was added dropwise over a period of 1 h. The resulting solution was stirred for 4 h while the temperature was maintained at 15–17°C. It was poured onto 400 g of crushed ice, and a

concentrated solution of technical sodium hydroxide (about 40%) was added until a pH of 5 was attained. The yellow precipitate was filtered and washed with 200 ml of water, followed by 400 ml of aqueous ammonia (5%). Then it was washed neutral with 1 liter of water and dried over phosphorus pentoxide, yielding 13·4 g of **3**. An analytical sample was prepared by chromatographic purification: a solution of 0·8 g was chromatographed on silica gel (Merck) using toluene/acetone (8:2) as eluent. The first fraction obtained was crystallized from methanol/acetonitrile (3:1) yielding 0·16 g of red crystals, m.p. 168–168·5°C (lit. 168–170°C)[2]. IR (cm^{-1}): 1767 (lactone), 1612 (aromat.), 1524 and 1349 (NO_2). ^{13}C-NMR (deuterioacetone) (selective decoupling) (ppm): 126·79 (C-4), 129·81 (C-5), 121·51 (C-7).

Analysis: Calcd for $C_{24}H_{23}N_3O_4$: C, 69·05, H, 5·55; N, 10·07. Found: C, 69·11; H, 5·52; N, 10·21%.

3,3′-Bis(*p*-dimethylaminophenyl)-6-aminophthalide (5)

A solution of crude **3** (36·61 g, 92%) in 750 ml of tetrahydrofuran (750 ml) was hydrogenated in the presence of Raney nickel (7·5 g) until hydrogen uptake ceased (found: 6372 ml; calcd: 6384 ml). The solvent was evaporated and the residue crystallized from a mixture of 90 ml of toluene and 45 ml of acetonitrile, yielding **5** (22·4 g, 61%); m.p. 223–224°C.[1] IR (cm^{-1}): 1612, 1522, 1503, 1329.

Analysis: Calcd for $C_{24}H_{27}N_3O_2$: C, 74·39; H, 6·50; N, 10·84. Found: C, 74·31; H, 6·70; N, 10·78%.

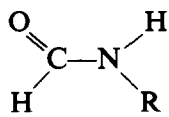
3,3′-Bis(3-nitro-4-dimethylaminophenyl)-6-nitrophthalide (6)

To a solution of 1·0 g (0·0027 mol) of **1** in 15 ml of concentrated sulfuric acid was added 3 ml of nitric acid (100%), and the mixture was stirred for 2 h. Then it was added to an excess of ice and adjusted to pH 4·5 by the addition of aqueous sodium hydroxide solution. The crystals were filtered and washed with water yielding **6** (1·28 g, 94%). Crystallization from methanol gave yellow crystals, m.p. 125–128°C. IR (cm^{-1}): 1767 (lactone), 1524 and 1349 (NO_2). ^{13}C-NMR (deuteriochloroform) (ppm): 149·33 (C-1), 125·45 (C-2), 118·42 (C-3), 146·34 (C-4), 127·20 (C-5), 129·48 (C-6), 90·34 (C-7), 169·23 (C-8), 137·45 (C-9), 127·08 (C-10), 125·06 (C-11), 155·90 (C-12), 149·33 (C-13), 131·62 (C-14).

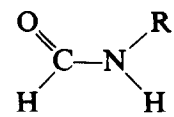
Analysis: Calcd for $C_{24}H_{21}N_5O_8$: C, 56·81, H, 4·17 N, 13·80. Found: C, 56·53, H, 4·21, N, 13·69%.

3,3'-Bis(*p*-dimethylaminophenyl)-6-*N*-formylaminophthalide (7)

A slurry of **5** (0·195 g, 5 mmol) in formic acid (3 ml) was heated to reflux for 2 min. The solution was evaporated to dryness and the crystalline residue stirred for 10 min with an aqueous solution (3 ml) of sodium hydrogen carbonate. The crystals were filtered and washed with water (10 ml) yielding **7** (0·172 g, 83%). IR (cm^{-1}): 1740 (lactone), 1698 (CHO), 1611. The NMR spectra showed that the compound consisted of a mixture of rotational isomers in the ratio of 28% of **7a** and 72% of **7b**.



7a



7b

3,3'-Bis(*p*-dimethylaminophenyl)-6-acetylaminophthalide (8)

A suspension of **5** (3·87 g, 1 mmol) in acetic anhydride (5·6 ml) was heated to 100°C for a period of 20 min. Then the solution was added to water (40 ml) and neutralized by addition of aqueous ammonia. The crystals were filtered and washed with water (40 ml) yielding **8**[1] (3·85 g, 89%). IR (cm^{-1}): 1762 (lactone), 1738 (C=O).

3,3'-Bis(*p*-dimethylaminophenyl)-6-propionylaminophthalide (9)

The compound was prepared from **5** and propionyl chloride according to the procedure detailed for **10**. IR (cm^{-1}): 1742 (lactone), 1612 (C=O).

3,3'-Bis(*p*-dimethylaminophenyl)-6-pivaloylaminophthalide (10)

To a solution of **5** (3·87 g, 10 mmol) in tetrahydrofuran (40 ml) was added triethylamine (1·52 g, 15 mmol) followed by pivaloic acid chloride (1·81 g, 15 mmol). The temperature was allowed to rise to 50°C. Then the solution was evaporated to dryness, and water (90 ml) and concentrated aqueous ammonia (10 ml) added. The oily suspension formed was heated to 60°C whereupon crystallization commenced. The crystals were filtered and dissolved in chloroform (100 ml). The chloroform solution was extracted with aqueous ammonia (5 ml, 2%), and dried over sodium sulfate. Evaporation of the solvent yielded **10** (4·8 g, 100%). IR (cm^{-1}): 1742 (lactone), 1524 (C=O).

3,3′-Bis(*p*-dimethylaminophenyl)-6-cinnamoylaminophthalide (11)

The compound was prepared from **5** and cinnamoyl chloride according to the procedure detailed for **10**. IR (cm^{-1}): 1745 (lactone), 1666 (C=O).

3,3′-Bis(*p*-dimethylaminophenyl)-6-benzoylaminophthalide (12)

The compound[1] was prepared from **5** and benzoyl chloride according to the procedure detailed for **10**. IR (cm^{-1}): 1760 (lactone), 1734 (C=O).

3,3′-Bis(*p*-dimethylaminophenyl)-6-(*p*-methoxybenzoyl)aminophthalide (13)

The synthetic procedure using **5** (10 mmol) followed the one detailed for **10**. IR (cm^{-1}): 1763 (lactone), 1736 (C=O).

3,3′-Bis(*p*-dimethylaminophenyl)-6-(*p*-trifluoromethylbenzoyl)aminophthalide (14)

The compound was prepared from **5** and 4-trifluoromethylbenzoyl chloride according to the procedure detailed for **10**. IR (cm^{-1}): 1736 (lactone), 1169, 1129 (both CF_3).

3,3′-Bis(*p*-dimethylaminophenyl)-6-(3,4,5-trimethoxybenzoyl)aminophthalide (15)

The compound was prepared from **5** and 3,4,5-trimethoxybenzoyl chloride according to the procedure detailed for **10**. IR (cm^{-1}): 1733 (lactone), 1613 (C=O).

3,3′-Bis(*p*-dimethylaminophenyl)-6-(2-thiophenoyl)aminophthalide (16)

The compound was prepared from **5** and 2-thiophene carboxylic acid chloride according to the procedure detailed for **10**; IR (cm^{-1}): 1736 (lactone), 1734 (CO).

3,3′-Bis(*p*-dimethylaminophenyl)-6-(methylsulfonyl)aminophthalide (17)

The compound was prepared from **5** and methanesulfonyl chloride in pyridine according to the procedure detailed for **18**. The non-crystalline crude product was purified by column chromatography as reported above for **8** to afford crystals of **17**. IR (cm^{-1}): 1763 (lactone), 1340, 1157 (SO_2N).

3,3′-Bis(*p*-dimethylaminophenyl)-6-(*p*-toluenesulfonyl)aminophthalide (18)

To a solution of **5** (1·16 g, 3 mmol) in pyridine (6 ml) was added *p*-toluenesulfonyl chloride (0·629 g, 3·3 mmol) and the mixture was allowed to stand

for 30 min at 25°C. Then the solution was added to water (30 ml) and the resinous product obtained was crystallized from acetonitrile (7 ml). IR (cm^{-1}): 1760 (lactone), 1335, 1161 (SO_2N).

3,3'-Bis(*p*-dimethylaminophenyl)-6-(*N,N*-dimethylureido)phthalide (19)

To a solution of **5** (1·94 g, 5 mmol) in pyridine (10 ml) was added dimethylcarbamoyl chloride (0·806 g, 7·5 mmol) and a temperature of 70°C was maintained for 6 h. The solvent was evaporated and water (30 ml) and aqueous ammonia (5 ml) were added to the residue. Filtration yielded 2·15 g crude product which was purified by chromatography as reported above for **8** to afford **19**. IR (cm^{-1}): 1743 (lactone).

3,3'-Bis(*p*-dimethylaminophenyl)-6-(ethylureido)phthalide (20)

To a solution of **5** (1·94 g, 5 mmol) in toluene (15 ml) was added ethyl isocyanate (0·71 g, 10 mmol) and the temperature was maintained at 80–100°C for 3 h. Then methanol (10 ml) was added and volatile products removed in a rotary evaporator. The residue was purified by chromatography as reported above for **8** to afford **20**. IR (cm^{-1}): 1736 (lactone), 1700 (C=O).

Dimethyl-6-*N*-3,3'-bis(*p*-dimethylaminophenyl)phthalidyl phosphoramidate (21)

A solution of **27** (4·17 g, 1 mmol) and trimethyl phosphite (2·48 g, 2 mmol) in toluene (30 ml) was heated to reflux for a period of 1 h. The solvent was evaporated and the residue dissolved in water (25 ml), and concentrated hydrochloric acid (5 ml) was added. Then the solution was neutralized with sodium carbonate, the precipitate filtered from the solution, washed with water and dried. The resinous product was crystallized from toluene yielding **21**. IR (cm^{-1}): 1758 (lactone), 1225 (P=O), 1062, 1037 (P—O).

3,3'-Bis(*p*-dimethylaminophenyl)-6-*N*-*tert.*-butyldimethyl)amino-phthalide (22)

A solution of **5** (1·16 g, 3 mmol), *tert.*-butyldimethylchlorosilane (1·5 g, 10 mmol) and triethylamine (1·01 g, 10 mmol) in tetrahydrofuran (10 ml) was heated to reflux for 72 h. Then the suspension was stirred with water (20 ml) and subsequently extracted three times each with chloroform (15 ml). The extracts were combined and purified in a manner analogous to that described for **8** to afford crystalline **22**. IR (cm^{-1}): 1736 (lactone), 836 [$(CH_3)_3$-Si$(CH_3)_2$].

3,3′-Bis(*p*-dimethylaminophenyl)-6-(*β*-cyanoethyl)aminophthalide (23)

A mixture of **5** (0·97 g, 2·5 mmol), acrylonitrile (0·8 g, 15 mmol) and acetic acid (0·1 ml) was placed in a sealed tube and heated to 150°C for a period of 24 h. The crude product was dissolved in methylene chloride (30 ml), washed with an aqueous solution of sodium hydrogen carbonate and dried (Na_2SO_4). Evaporation of the solution left a yellow oil (1·05 g) which was purified in a manner analogous to that described for **10** to afford a viscous residue which was crystallized from toluene. IR (cm^{-1}): 2248 (CN), 1739 (lactone).

3,3′-Bis(*p*-dimethylaminophenyl)-6-*N*-(*β*-ethylcarboxymethyl)phthalide (24)

A mixture of **5** (0·97 g, 2·5 mmol), methyl acrylate (1·34 g, 15 mmol) and acetic acid (0·1 ml) was placed in sealed tube and heated to 150°C for a period of 14 h. The work-up and the purification were performed in a manner analogous to that described for **10**. IR (cm^{-1}): 1740 (lactone), 1612 ($COOCH_3$).

3,3′-Bis(*p*-dimethylaminophenyl)-6-(*N*-pyrrolyl)phthalide (25)

A mixture of **5** (3·87 g, 10 mmol), 2,5-dimethoxytetrahydrofuran (1·32 g, 10 mmol) and acetic acid (6 ml) were refluxed for 15 min. The work-up and the purification procedure were performed in a manner analogous to that described for **10** to afford **25** as an oil. Crystallization from acetonitrile gave a crystalline analytical sample. IR (cm^{-1}): 1763 (lactone).

3,3′-Bis(*p*-dimethylaminophenyl)-6-*N*-(2,5-dimethylpyrrolyl)phthalide (26)

To a mixture of **5** (3·87 g, 10 mmol) and acetonylacetone (2·85 g, 25 mmol) was added one drop of 4 M-hydrochloric acid. The suspension was heated to reflux for 1·5 h. The viscous oil formed was purified by column chromatography as reported above for **8** to afford **26** as an oil. Crystallization from acetonitrile furnished a crystalline product. IR (cm^{-1}): 1764 (lactone).

3,3′-Bis(*p*-dimethylaminophenyl)-6-azidophthalide (27)

To a solution of **5** (3·89 g, 1 mmol) in water (35 ml) and hydrochloric acid (5 ml) was added at 0°C over a period of 10 min a solution of sodium nitrite (0·75 g, 11 mmol) in water (2 ml). It was stirred for an additional 30 min and the excess of nitrite destroyed by adding sulfaminic acid. Then a solution of sodium azide (0·975 g, 20 mmol) in water (3 ml) was added. The temperature was allowed to rise to 30°C until nitrogen evolution had ceased, and then the mixture was added to an aqueous solution of sodium hydrogen carbonate

(40 ml). The crystals were filtered and dried yielding **27** (3·74 g, 91%). An analytical sample was recrystallized from toluene–acetonitrile. IR (cm^{-1}): 2114 (N_3), 1763 (lactone).

3,3'-Bis(*p*-dimethylaminophenyl)-6-[1-*N*-4,5-bis(methylcarbamoyl)]-1,2,3-triazolyl phthalide (28)

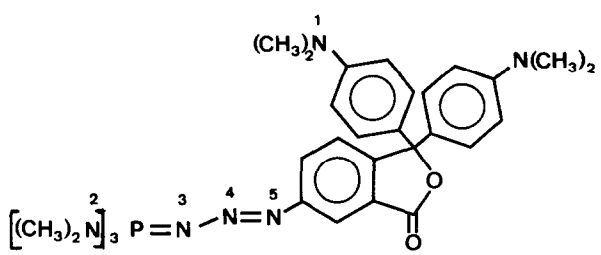
A solution of azide **27** (1·03 g, 2·5 mmol) and dimethyl acetylenedicarboxylate (0·568 g, 4 mmol) in toluene (7 ml) was heated to 80°C for 20 h. The oily product was purified by column chromatography as reported above for **10** to afford 2·2 g of **28** as a viscous oil. Crystallization from toluene (7 ml) gave crystals of **28**. IR (cm^{-1}): 1769 (lactone), 1739 (ester).

3,3'-Bis(*p*-dimethylaminophenyl)-6-*N*(triphenylphosphazo)phthalide (29)

To a solution of **27** (1·03 g, 2·5 mmol) in toluene (15 ml) was added triphenylphosphine (0·72 g, 2·7 mmol) and the mixture was heated to 60°C for 30 min. The warm solution was filtered, and crystals allowed to precipitate. Filtration furnished **29**. IR (cm^{-1}): 1747 (lactone), 1356 (P=N).

3,3' -Bis(*p*-dimethylaminophenyl)-6-*N*-{[tris(dimethylamino)]phosphazo-triazenyl}phthalide (30)

To a suspension of **27** (4·13 g, 10 mmol) in toluene (25 ml) was added tris(dimethylamino)phosphine (2·45 g, 15 mmol). The crystals dissolved and an orange-colored suspension was formed. Filtration yielded crystals (5 g) which were washed with toluene (5 ml). Crystallization from a mixture of toluene (15 ml) and acetonitrile (12·5 ml) furnished **30**. Mass spectrum: 548. ^{14}N-NMR ($CDCl_3$) (ppm): 44·92 (N-1), 20·64 (N-2) (J_{NP} = 23 Hz), 249·25 (N-3) (J_{NP} = 34 Hz), 382·34 (N-4) (J_{NP} = 27·5 Hz), 514·25 (N-5) (J_{NP} = 20 Hz). ^{31}P-NMR ($CDCl_3$): 42·73. IR (cm^{-1}): 1753 (lactone), 1361 (P=N).



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3,3′-Bis(*p*-dimethylaminophenyl)-6-(*N*-methyl-*N*-toluenesulfonyl)-phthalide (31)

A suspension of **18** (0·27 g, 5 mmol) and potassium carbonate (0·07 g) in dimethyl methylphosphonate (5 ml) was heated to reflux for 4 h. Then the solution was added to water (25 ml), and the crystals were filtered and washed with water (10 ml) yielding **31**. IR (cm^{-1}): 1759 (lactone), 1349 and 1171 (SO_2N).

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