

Phthalocyanine-modified silica gels and their application in the purification of unsymmetrical phthalocyanines

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Five species of phthalocyanine-modified silica gels were prepared. The loadings of phthalocyanine on these silica gels were determined by acidic hydrolysis. The concept of using the aggregation phenomenon to advantage to aid chromatographic separation of unsymmetrical phthalocyanines was investigated by employing these modified silica gels as chromatographic media to purify unsymmetrical phthalocyanines. Four groups of phthalocyanine mixtures were prepared by mixed condensation. One of the desired unsymmetrical phthalocyanines was successfully purified by conventional column chromatography while others were separated by the new method described herein.

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On a préparé cinq espèces de gels de silice modifiés par des phthalocyanines. On a déterminé la quantité de phthalocyanine présente sur ces gels de silice en faisant appel à une hydrolyse acide. On a étudié le concept de l'utilisation du phénomène d'aggrégation pour faciliter la séparation chromatographique de phthalocyanines non symétriques en utilisant ces gels de silice modifiés comme milieux chromatographiques pour la purification de phthalocyanines non symétriques. On a préparé quatre groupes de mélanges de phthalocyanines par condensations mixtes. On a réussi à purifier une des phthalocyanines non symétriques désirées par chromatographie conventionnelle sur colonne alors que les autres ont été séparées par la méthode décrite ici.

[Traduit par la rédaction]

Unsymmetrical phthalocyanines present challenges in the development of new methods of synthesis and separation. The potential use of phthalocyanines for photodynamic therapy (PDT) of cancer has sparked considerable interest in the photobiology of these compounds (1–9). To find a suitable phthalocyanine as photosensitizer, it is necessary to tune the position of its absorption band. Such fine tuning can be achieved by the stepwise introduction of peripheral substituent groups or by the stepwise adjustment of the size of the π -conjugated macrocyclic systems (10–13). Thus, unsymmetrical phthalocyanines are important goals in synthesis. Although symmetrical tetra- and octasubstituted phthalocyanines are well known, the synthesis of simple mono- and disubstituted and other unsymmetrical phthalocyanines remains a difficult problem (10–21). For instance, all tetrasubstituted phthalocyanines so far synthesized contain one substituent in each of the benzene rings, and no phthalocyanines such as 1,2,3,4- or 1,2,3,8-tetrasubstituted phthalocyanines have been reported.

Successful methods for the synthesis of unsymmetrical phthalocyanines can be divided into three groups according to strategy: (1) the polymer support route (14, 16, 19, 20); (2) the homogeneous mixed condensation route (12–14, 21); and (3) the subphthalocyanine route (11). There are difficulties with all three routes for large-scale preparation of unsymmetrical alkoxy-substituted phthalocyanines.

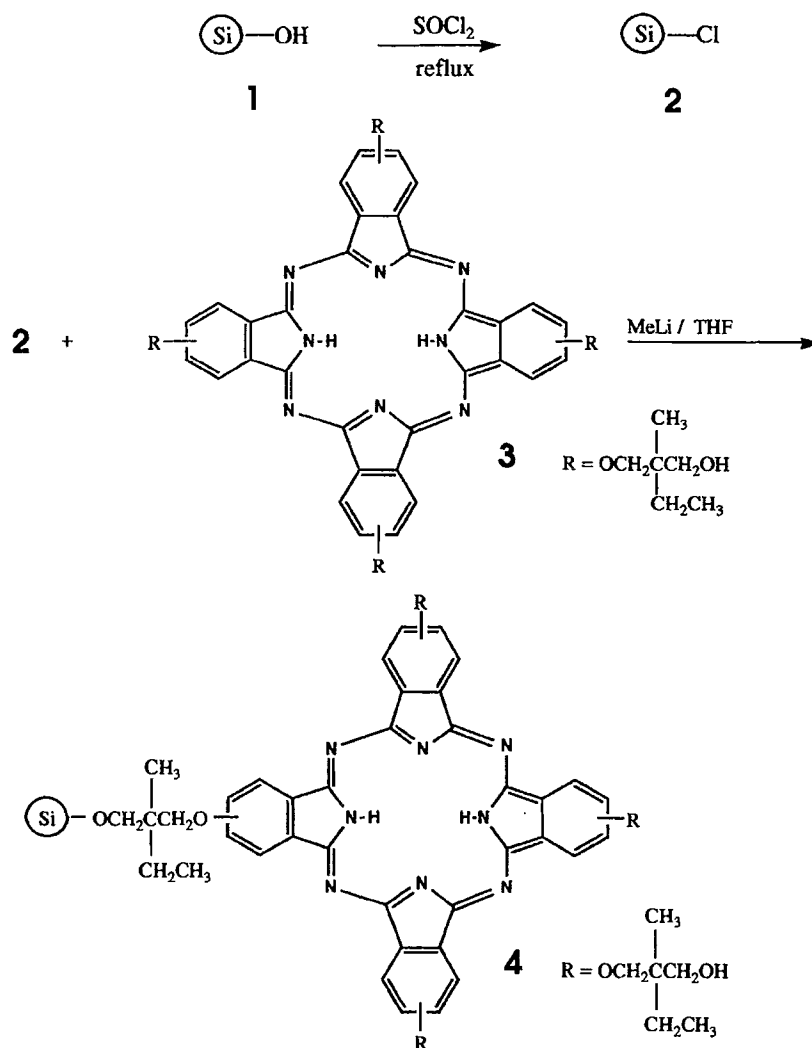
Route 1 is not suitable for large-scale preparation of unsymmetrical phthalocyanines. Route 3 is not suitable for the preparation of alkoxy-substituted phthalocyanines, as this method uses BBr_3 , an ether-cleaving reagent. Route 2, the ordinary method of forming unsymmetrical phthalocyanines by mixed condensation of different phthalonitriles, most often gives statistical mixtures of phthalocyanines, which are very difficult to separate by common chromatographic methods. Although purifications of desired unsymmetrical phthalocyanines from mixed condensations by

common chromatographic methods have been reported, success has been achieved only with those phthalocyanines having greatly differing polarities and after numerous repetitions of chromatographic separations. There appear to be two reasons for such difficulties. First, a number of very similar phthalocyanine species exist in the mixture. With site-isomers considered, a mixture from a mixed condensation conceivably can contain more than 20 species of similar phthalocyanines! Second, strong aggregation (22–24) exists among the different phthalocyanine species. Generally speaking, one of the basic premises and presumptions of chromatography is that each gradient to be separated should behave independently without interfering with another. The premise is not valid if aggregation occurs. Thus, a well-defined band on column chromatography or a single spot on thin-layer chromatography (TLC) is by itself insufficient evidence of purity and should be accompanied by mass spectral and other spectroscopic data (15).

In this investigation, the homogeneous mixed condensation route was used, together with work aimed at developing a more powerful method of separation. For the latter, we envisioned and investigated a new strategy which *takes advantage of the aggregation* that would be expected to occur between immobilized phthalocyanines and those in the synthetic mixture.

Five species of phthalocyanine-modified silica gels (Pc-Si-Gels) were prepared. These Pc-Si-Gels can be divided into three groups. In the first group, flash grade silica gel (1), preactivated with concentrated hydrochloric acid (25), reacted with thionyl chloride to give chlorinated silica gel (2). A reaction between 2 and 2,9,16,23-tetrakis(2-hydroxy-methyl-2-methylbutoxy)phthalocyanine (3) (14) gave a modified silica gel (4), which contained phthalocyanine entities bonded to silica through Si—O—C linkages (Scheme 1). It should be noted that the phthalocyanine entities could be bonded to silica through more than one Si—O—C linkage (26), so its structure shown in Scheme 1 represents a simplified model.

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SCHEME 1

In the second group of Pc-Si-Gels, the metal atoms of metallophthalocyanines are bonded with the oxygen atoms of silica gels (Scheme 2). Thus, reactions of 2,9,16,23-tetra-*tert*-butylphthalocyanine (5) (27), 2,9,16,23-tetraneopentoxypthalocyanine (6) (28), or unsubstituted phthalocyanine (7) with trimethyl aluminum and 1 gave 2,9,16,23-tetra-*tert*-butylphthalocyaninato aluminum(III) silica (8), 2,9,16,23-tetraneopentoxypthalocyaninato aluminum(III) silica (9), or phthalocyaninato aluminum(III) silica (10), respectively.

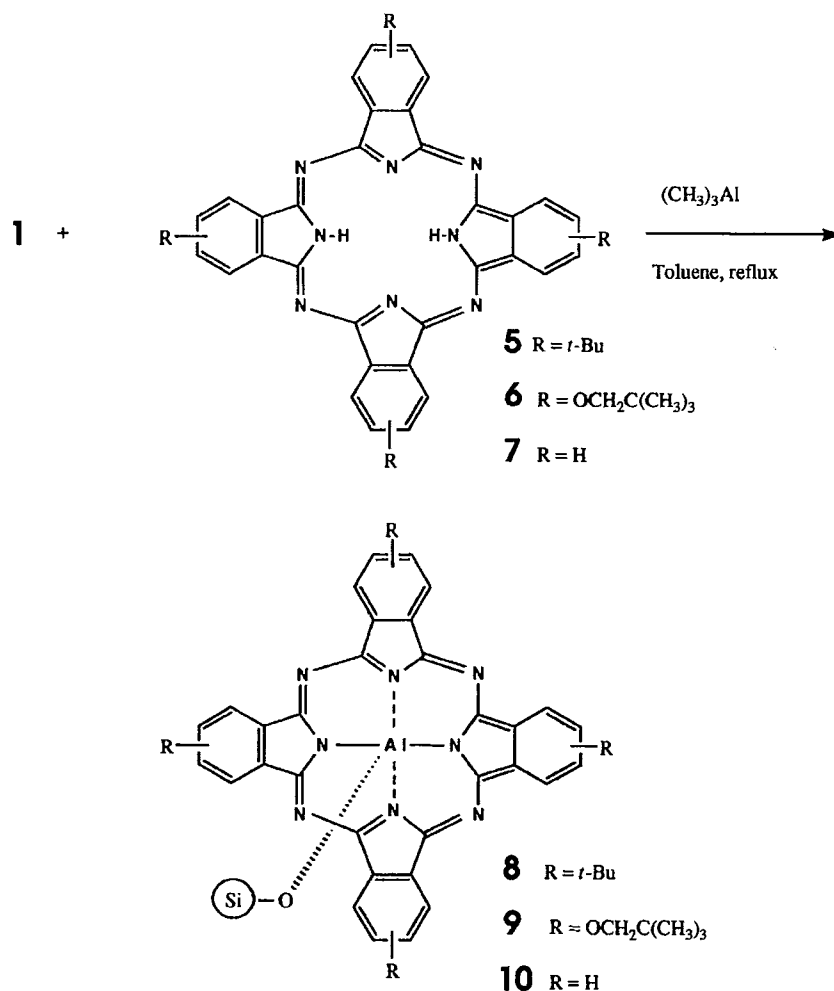
In the third group, the metal atom of the phthalocyanine is bonded to the nitrogen atom of an aminopropyl derivative of silica (29) (Scheme 3). During the process of preparation, 1 reacted with (3-aminopropyl)trimethoxysilane (11) to give 3-aminopropylsilyl silica (12), which then reacted with methylaluminum(III) phthalocyanine (13) and gave phthalocyaninato aluminum(III) aminopropylsilyl silica (14).

To determine the loadings of immobilized Pc in the Pc-Si-Gels, three accurately weighed samples of each of the Pc-Si-Gels were hydrolysed with hydrochloric acid. Comparison of the UV spectra of the filtrates with reference solutions, also under acidic conditions, gave the values of the loadings, which are summarized in Table 1. In all examples the silica gels recovered from acidic hydrolyses were colourless and

indeed hydrolyses were continued until the silica gels were colourless. Three species of the Pc-Si-Gels, namely 4, 9, and 14, were chosen to pack columns. One of the Pc-Si-Gels, 4, was abandoned as it was found to be unstable in the alcoholic solvent (2-methoxyethanol:toluene = 4:6) used in the column-cleaning process. Among the Pc-Si-Gels 8–10, compound 8 was formed in lower yield while 10 was abandoned in favour of 14, a chain-extended analog of 10, and hence 8 and 10 were not examined further.

Four homogeneous mixed condensations were used to prepare mixtures of unsymmetrical phthalocyanines. The mixed condensation of 2,3-dihydro-1,3-diimino-1*H*-benz[*f*]isoindole (15) with 5-neopentoxo-1,3-diiminoisoindoline (16) or 5-*tert*-butyl-1,3-diiminoisoindoline (17) gave mixtures containing 2,9,16-trineopentoxo-31*H*,33*H*-tribenzo[*b,g,l*]-naphtho[2,3-*q*]porphyrizine (18) or 2,9,16-tri-*tert*-butyl-31*H*,33*H*-tribenzo[*b,g,l*]-naphtho[2,3-*q*]porphyrizine (19) (Scheme 4). The mixed condensation of 16 and 17 gave a mixture containing 2-*tert*-butyl-9,16,23-trineopentoxypthalocyanine (20) (Scheme 5). The mixed condensation of 4,5-di-(1-octyn-1-yl)phthalonitrile (21)² and 4-methoxy-

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SCHEME 2

methoxyphthalonitrile (**22**) (**30**) with DBU and zinc acetate gave a mixture containing 2,3-di-(1-octyn-1-yl)-9,16,26-tri-(methoxymethoxy)phthalocyanine zinc(II) (**23**) (Scheme 6).

Among those desired phthalocyanines, **23** was successfully purified by ordinary column chromatography with the help of reverse phase HPLC as a monitor. The other three species, **18**, **19**, and **20**, could not be completely purified by ordinary column chromatography, but were successfully purified by Pc-Si-Gel column chromatography with the help of reverse phase HPLC or UV as a monitor.

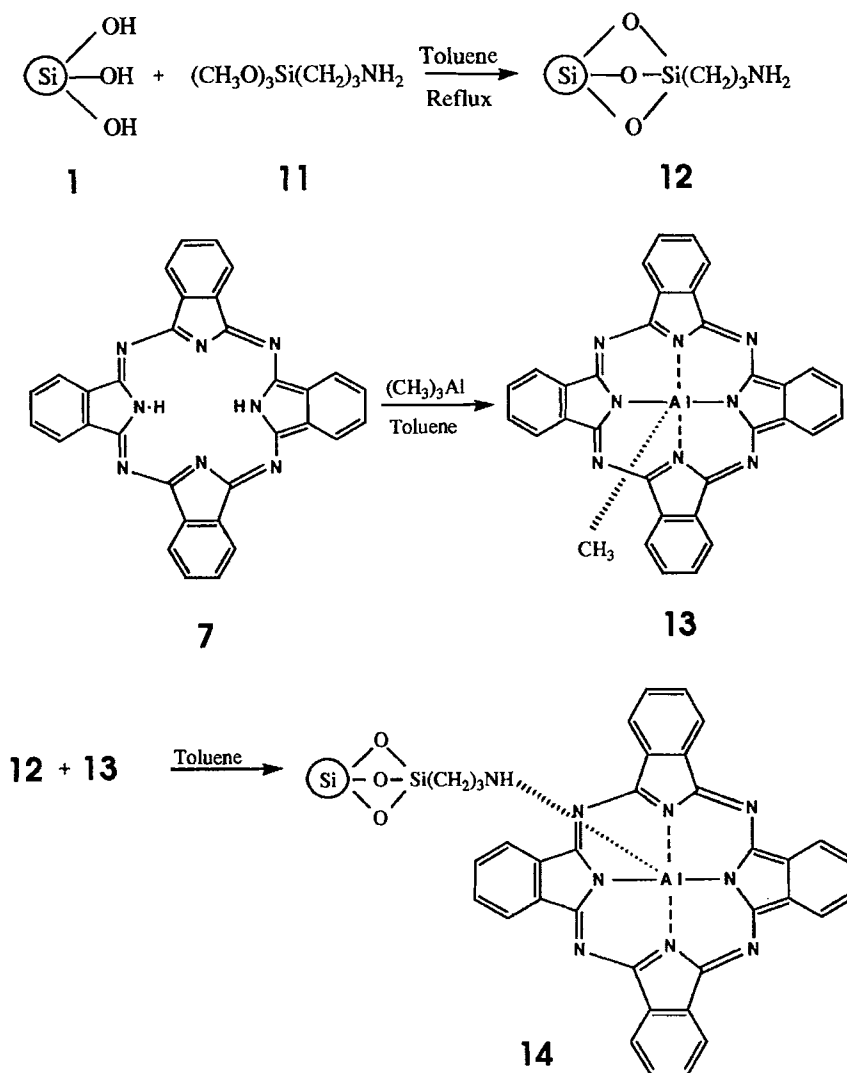
The mass spectra and other data showed that complete separations were achieved. For instance, the mass spectrum of **18** showed that none of the phthalocyanines (porphyrazines) containing di-, tri-, or tetrabenz groups or tetraeneopentoxypthalocyanines contaminated the desired unsymmetrical phthalocyanine. As a comparison, the same crude products were subjected to ordinary flash chromatography for as many as four repetitive columns. Even so, the mass spectra of the purest fractions showed that substantial contamination by undesired phthalocyanines still occurred (e.g., m/z 858, tetraeneopentoxypthalocyanine; 786, dibenzodineopentoxypthalocyanine (dibenzodinaphthoporphyrazines)).

It should be noted that each of the unsymmetrical phthalocyanines (**18**–**20**, **23**) are likely a mixture of several closely related site-isomers. So far, we have not seen any successful example of the separation of such phthalocyanine isomers by chromatographic methods. This method does not readily separate similar isomers such as 2,9,16,23-, 2,10,16,24-, 2,9,17,24-, and 2,9,16,24-tetraeneopentoxypthalocyanine (**6**) and this mixture has normally been represented as the 2,9,16,23 isomer.

The experiments showed that the Pc-Si-Gels have some enhanced ability relative to standard silica gel for the purification of phthalocyanines. The separation ability of Pc-Si-Gels may depend on a number of complicated factors: amongst others, the nature of the phthalocyanines to be separated, the solvent system employed, and the chemical nature and physical condition of the phthalocyanines bonded to the polymer. Further studies of this new strategy are required before a general statement in this regard can be made. As well, additional work will be aimed at further enhancement of the capabilities of Pc-Si-Gels in practical applications.

Experimental

High-purity argon was used to maintain inert atmosphere conditions. Infrared (IR) spectra were recorded on a Pye Unicam SP-3200 infrared spectrophotometer using KBr discs for solids or



SCHEME 3

TABLE 1. Some properties of Pc-Si-Gels

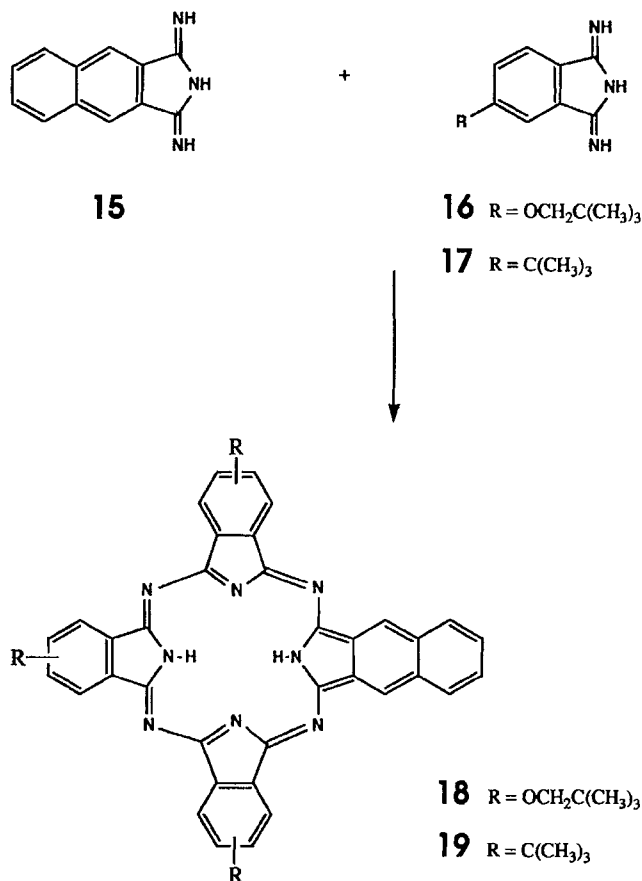
Pc-Si-Gels	Pc loading (mg/g) (mmol/g)	Yield ^a (%)	Colour
4	18.7 (0.020)	66.5	Dark green
8	14.4 (0.019)	47.0	Dark blue
9	28.7 (0.033)	~100	Dark green
10	22.3 (0.044)	55.6	Dark blue
14	29.9 (0.056)	~100	Dark blue-grey

^aUsually, the functional groups on silica gel are used as the limiting reagents, but in these cases, since the functional groups on silica gel were in excess, the yields were calculated using the phthalocyanines as the limiting reagents.

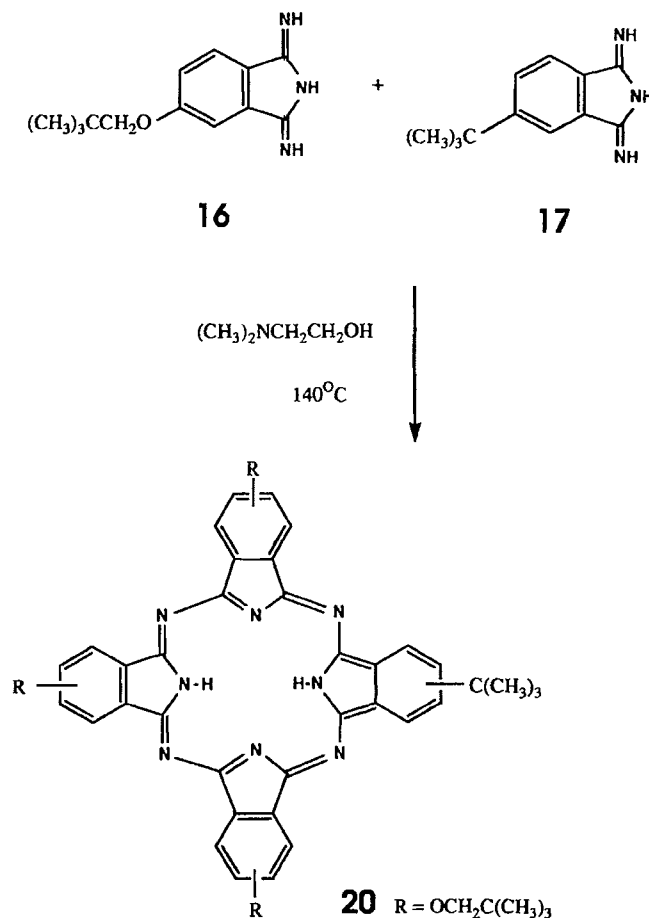
as neat films between NaCl discs for liquids. Nuclear magnetic resonance (NMR) spectra for carbons and protons were recorded on a Bruker AM300 NMR spectrometer using tetramethylsilane as the internal standard. The positions of the signals are reported in δ units. The splittings of the signals are described as singlets (s), doublets (d), triplets (t), quartets (q), or multiplets (m). The ^1H NMR spectra of 10^{-4} M solutions of the phthalocyanines were obtained by averaging 500–3000 scans over the absorption range. The ^{13}C NMR spectra of 5×10^{-4} M solutions of the phthalocyanines were obtained by averaging 7000–15 000 scans. The ultraviolet–

visible spectra (UV–VIS) were recorded on a Hewlett Packard HP8451A diode array spectrophotometer. Mass spectra (MS) were recorded at 70 eV on a VG Micromass 16F mass spectrometer in the EI mode for relatively small molecules (generally less than 800 amu). The Fast Atom Bombardment mode (FAB) spectra were obtained with a Kratos Profile or Kratos MS-50 analyzer mass spectrometer equipped with a FAB ion source of standard Kratos design and Ion Tech atom gun for relatively large molecules (generally greater than 800 amu).

Melting points (mp) were determined using a Kofler hot stage



SCHEME 4



SCHEME 5

melting point apparatus and are uncorrected. Thin-layer chromatography (TLC) was performed using Kodak 13181 silica gel TLC sheets unless otherwise stated. Flash chromatography was performed using silica gel of particle size 20–45 μm (purchased from Terochem Laboratories Ltd., equivalent to Merck 9385). Neutral alumina column chromatography was performed using Brockmann I standard grade (150 mesh, 155 m^2/g). Reaction mixtures were stirred with a magnetic stirrer, except those that required sonication. Ultrasound treatment was carried out using a Branson 1200 sonicator. Microanalyses were performed by Guelph Chemical Laboratories Ltd., Guelph, Ont. All diiminoindolines were used directly without purification, after evaporation of the solvent in condensation experiments. All yields were not optimized by detailed investigation of the effects of temperature, reaction time, and other conditions.

Activated flash silica gel (1)

Flash grade silica gel (20–45 μm , purchased from Terochem Laboratories Ltd.) was heated under reflux with concentrated hydrochloric acid for 4 h. The ratio of concentrated hydrochloric acid to **1** was 4–5 mL/g. After cooling to room temperature, **1** was filtered, washed with distilled water until the filtrate was neutral, preliminarily dried in an oven, and thoroughly dried under vacuum (140°C, 0.05 Torr (1 Torr = 133.3 Pa), 3 h).

Chlorinated silica gel (2)

Freshly distilled thionyl chloride (30 mL) was injected into a round-bottom flask that contained 5.7 g of **1** under argon. After heating under reflux with stirring for 24 h, the mixture was filtered under argon in a Schlenk tube. After washing with dry dichloromethane (20 mL, three times) by injection, the chlorinated silica gel was obtained as a white powder.

To determine the chlorine loading, three accurately weighed

samples of **2** (about 50 mg each) were taken out and immediately treated with 10 mL of distilled water with stirring. After 10 min, the suspensions were titrated with a 0.1 M aqueous solution of potassium hydroxide and compared with a blank assay. The chlorine loadings were determined to be $\sim 1.0 \pm 0.1$ mmol per gram of silica gel. Different batches of silica gel yielded chlorine loadings of 0.8–1.8 mmol/g.

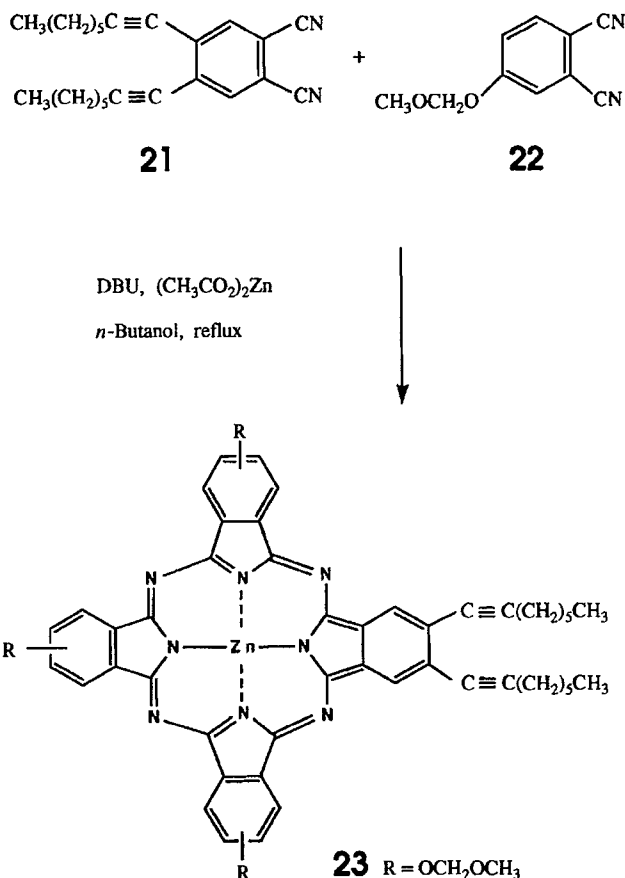
2,9,16,23-Tetrakis(2-hydroxymethyl-2-methylbutoxy)phthalocyanine (3) modified silica gel (4)

A solution of **3** (162 mg, 0.17 mmol) (**14**) in 30 mL of dry tetrahydrofuran (THF) and 0.5 mL of 1.4 M methyllithium solution in toluene was injected into a round-bottom flask that contained 5.7 g of **2**. The mixture was stirred at room temperature for 24 h. After filtering and washing with dry toluene and dry THF (three times each), a dark green powder of Pc-Si-Gel **4** was obtained.

To determine the loading of phthalocyanine on silica gel, three accurately weighed samples of **4** (about 50 mg each) were hydrolyzed in 10 mL of hydrochloric acid solution (HCl:THF:H₂O = 1:8:1) by heating under reflux for 1 h, and then were filtered. Comparison of the UV–VIS spectra of the filtrate with a solution of **3** as a reference showed that the loading of phthalocyanine on **4** was 18.7 mg per gram of silica gel (0.020 mmol/g). The yield was 66% with **3** as the limiting reactant.

2,9,16,23-Tetra-tert-butylphthalocyaninatoaluminum(III) silica (8)

Trimethylaluminum (8.5 mL of 2 M solution in toluene) was injected into a round-bottom flask that contained 8.5 g of **1** and 30 mL of dry toluene under argon. The suspension was stirred at room temperature overnight, then filtered and washed once with



SCHEME 6

dry toluene. A solution of 2,9,16,23-tetra-*tert*-butylphthalocyanine (**5**) (**27**) (260 mg, 0.35 mmol) in 40 mL of dry toluene was then injected. The reaction was monitored by removal of an aliquot and examination by UV-VIS spectroscopy to ensure that all of **8** was consumed. The suspension was stirred under reflux for 48 h, at which time the reaction was complete, and then was filtered. The dark blue powder was first washed with dry toluene until the solvent was almost colourless, then washed with dry THF three times, with dry dichloromethane three times, and dried in the air.

Three accurately weighed samples (about 50 mg each) were hydrolysed by heating under reflux for 2 h with 10 mL of hydrochloric acid solution (HCl:THF:H₂O = 1:8:1). After filtration, the comparison of the UV-VIS spectrum of the filtrate with that of a similar acidic reference solution of the starting material **5** showed that the loading of **5** on **8** was 14.4 mg per gram of silica gel (0.019 mmol/g). The yield was 47% with **5** as the limiting reactant.

2,9,16,23-Tetraneopentoxypthalocyaninatoaluminum(III) silica (**9**)

Trimethylaluminum (6.0 mL of 2 M solution in toluene) was injected under argon into a round-bottom flask that contained 6.0 g of **1** and 25 mL of dry toluene. The suspension was stirred at room temperature overnight, then filtered and washed once with dry toluene. A solution of 2,9,16,23-tetraneopentoxypthalocyanine (**6**) (**28**) (168 mg, 0.20 mmol) in 30 mL of dry toluene was then injected. The suspension was stirred under reflux for 48 h until the reaction was complete (as monitored for **8** above) and then was filtered. The filtrate was almost colourless. The dark green powder was then washed with dry toluene three times, with dry THF three times, with dry dichloromethane three times, and dried in the air. Three accurately weighed samples (about 50 mg each) were

taken and hydrolysed by heating under reflux for 2 h with 10 mL of hydrochloric acid solution (HCl:THF:H₂O = 1:8:1). After filtration, comparison of the UV-VIS spectrum of the filtrate with that of a reference solution of the starting material **6** showed that the loading of **6** on **9** was 28.7 mg per gram of silica gel (0.033 mmol/g). The yield was 100% with **6** as the limiting reactant.

Phthalocyaninatoaluminum(III) silica (**10**)

Unsubstituted phthalocyanine **7** (1.28 g, 2 mmol) was mixed with 50 mL of a 1.9 M solution of trimethylaluminum in toluene under argon. This mixture was treated with ultrasound for 24 h to improve solubility and then filtered through a Schlenk tube into a flask containing 24 g of **1**. After heating under reflux for 48 h under argon, the mixture was filtered in the Schlenk tube and washed with dry toluene and dry dioxane. The dark blue modified silica gel was then treated with dry dioxane, which allowed the unbound unsubstituted phthalocyanine to be removed by floatation. After the floatation procedure was repeated a few times, no visible unbound phthalocyanine remained and the Pc-Si-Gel **10** was obtained as a dark blue powder.

To determine the loading of **7** on **10**, three accurately weighed samples of **10** (about 50 mg each) were taken and hydrolysed by heating for 2 h under reflux with 10 mL of hydrochloric acid solution (HCl:THF:H₂O = 1:8:1). After filtration, comparison of the UV-VIS spectrum of the filtrate with that of an acidic reference sample, which was prepared by hydrolysis of **13** and diluted to a suitable concentration for the UV-VIS spectrum, showed that the loading of **7** on **10** was 22.3 mg per gram of silica gel (0.044 mmol/g). The yield was 55.6%, with **7** as the limiting reactant.

3-Aminopropylsilyl silica (**12**)

Activated dry silica gel (**1**, 55 g) was mixed with 30 mL (160 mmol) of (3-aminopropyl)trimethoxysilane (**11**) and 250 mL of dry toluene. The suspension was stirred under reflux overnight, and then filtered. The solids were washed with dry toluene and anhydrous ether to give **12**.

To determine the amino group loading, three accurately weighed samples (about 50 mg each) were treated with 5 mL of 0.05 M aqueous solution of sulphuric acid for 10 min, then filtered and titrated with a 0.1 M aqueous solution of potassium hydroxide. Comparison with a blank assay showed that the amino loading on **12** was 0.8–1.3 mmol per gram of silica gel.

Phthalocyaninato methylaluminum(III) (**13**)

A mixture of 1.6 g (3.1 mmol) of metal-free unsubstituted phthalocyanine **7**, 10 mL of a 1.9 M solution of trimethylaluminum (19 mmol) in toluene, and 100 mL of dry toluene was treated with ultrasound for 24 h to give a solution of phthalocyaninato methylaluminum(III) **13**. Without purification and characterization, **13** was used to prepare **14** immediately.

Phthalocyaninatoaluminum(III) aminopropylsilyl silica (**14**)

The newly prepared **12** (55 g) and 100 mL of dry toluene were poured with vigorous stirring into a round-bottom flask containing 110 mL of a hot solution of **13** under argon. After heating under reflux for 1 h, at which time reaction was complete (as monitored for **8** above), the suspension was filtered to give a dark blue-grey powder and an almost colourless filtrate. The powder was then washed with dry toluene three times, followed by dry dioxane three times, to give **14**.

To determine the phthalocyanine loading on **14**, three accurately weighed samples of **14** (about 50 mg each) were taken and hydrolysed by heating for 1 h under reflux with 10 mL of hydrochloric acid solution (HCl:THF:H₂O = 1:8:1). After filtration, comparison of the UV-VIS spectrum of the filtrate with that of an acidic reference sample, prepared by hydrolysis of **13** and diluted to a suitable concentration for the UV-VIS spectrum, showed that the loading of **7** was 29.0 mg per gram of **14** (0.056 mmol/g). The yield was ~100% with **7** as the limiting reactant.

2,9,16-Tri-*n*-pentoxo-3*H*,33*H*-tribenzo[*b,g,l*]naphtho[2,3-*q*]porphyrizine (18)

A solution of **15** derived from 178 mg (1 mmol) of 2,3-dicyanonaphthalene (**12**) (Tokyo Kasei) and **16** derived from 642 mg (3 mmol) of 4-*n*-pentoxophthalonitrile (**15**) (**28**) in 4 mL of 2-*N,N*-dimethylaminoethanol was heated under reflux for 48 h. The dark green mixture was then poured into 100 mL of water, and the precipitate was filtered and washed with methanol a few times until the filtrate was colourless. After flash chromatography with toluene as solvent, 356 mg of a phthalocyanine mixture was obtained in about 43.5% yield. The phthalocyanine mixture was then subjected to common flash silica gel chromatography using carbon tetrachloride/toluene (30/0–70/100) as the eluting solvent, while monitoring with UV–VIS spectroscopy, to afford crude **18**. Further purification was effected by column chromatography with **14** or **9** as the static phase. After evaporation of the solvent and precipitation from methanol, the desired 2,9,16-tri-*n*-pentoxo-3*H*,33*H*-tribenzo[*b,g,l*]naphtho[2,3-*q*]porphyrizine (**18**, 104.5 mg) was obtained, in 12.7% yield, as a purple solid; IR (KBr, cm^{-1}): 3300 (w, NH), 1620 (vs, C=C), 1240 (s, COC), 1100 (s, COC), 1020 (vs, NH), 750 (s, CH_{arom}); UV–VIS (1,2-dichlorobenzene, nm) (log ϵ): 734 (5.00), 690 (4.94), 670 (4.70), 622 (4.22), 400 (4.49), 344 (4.72), 300 (4.51); ^1H NMR (CDCl_3) δ : 7.0–9.1 (vbr, aromatic), 4.0–4.2 (m, $-\text{OCH}_2\text{C}-$, 6H), 1.1–1.6 (m, $-\text{CH}_3$, 27H), -3.6 (br N-H); ^{13}C NMR (toluene- d_8) δ : 116–162 (C_{arom}), 78 (CH_2O), 27.2 ($\text{C}-\text{CH}_3$), 19.7–21.2 ($\text{C}-\text{CH}_3$); MS (FAB) m/z : 823 ($\text{M}^+ + 1$, 100%), 752 (19%), 681 (9%). Anal. calcd. for $\text{C}_{51}\text{H}_{50}\text{N}_8\text{O}_3$: C 74.42, H 6.12, N 13.61; found: C 73.84, H 6.32, N 13.26.

The mass spectrum of **18** showed no contamination by undesired phthalocyanines. As a comparison, the same crude product was subjected four times to ordinary flash silica gel chromatography. The mass spectrum of its purest components indicated that it still contained some 2,9,16,23-tetra-*n*-pentoxophthalocyanine.

2,9,16-Tri-*tert*-butyl-3*H*,33*H*-tribenzo[*b,g,l*]naphtho[2,3-*q*]porphyrizine (19)

A solution of **15** derived from 178 mg (1 mmol) of 2,3-dicyanonaphthalene (Tokyo Kasei) and **17** derived from 552 mg (3 mmol) of 4-*tert*-butylphthalonitrile (**27**) (Tokyo Kasei) in 4 mL of 2-*N,N*-dimethylaminoethanol was heated under reflux for 48 h. The dark blue mixture was then poured into 100 mL of water to form a precipitate. The precipitate was filtered and washed with methanol a few times until the filtrate was colourless. After column chromatography with ordinary flash silica gel as the static phase and toluene as the eluting solvent, 198 mg of a phthalocyanine mixture was obtained in about 27% yield. The phthalocyanine mixture was then separated again by flash silica gel chromatography to get the crude **19**. Further purification was effected by column chromatography with Pc-Si-Gel **14** or **9** as the static phase, with carbon tetrachloride/toluene (70/30–0/100) as the eluting solvent and using UV–VIS spectroscopy as a monitor. After evaporation of the solvent and precipitation from methanol, 52.8 mg of pure 2,9,16-tri-*tert*-butyl-3*H*,33*H*-tribenzo[*b,g,l*]naphtho[2,3-*q*]porphyrizine (**19**) was obtained, in 7.2% yield, as a purple solid, IR (KBr, cm^{-1}): 3300 (w, NH), 1620 (vs, C=C), 1010 (vs, NH), 750 (s, CH_{arom}); UV–VIS (1,2-dichlorobenzene, nm) (log ϵ): 730 (5.10), 686 (5.09), 666 (4.82), 618 (4.47), 346 (4.85), 302 (4.52); ^1H nmr (toluene- d_8) δ : 6.9–8.1, 8.6–9.5 (vbr, aromatic), 1.7–1.8 (m, $-\text{CH}_3$, 27 H), -2.3 (br N-H); ^{13}C nmr (toluene- d_8) δ : 122.5–152.8 (C_{arom}), 35.8–36.0 ($\text{C}-\text{CH}_3$), 32.1–32.3 ($\text{C}-\text{CH}_3$); MS m/z : 733 ($\text{M}^+ + 1$, 100%), 718 (22%), 703 (9%), 676 (17%). Anal. calcd. for $\text{C}_{48}\text{H}_{44}\text{N}_8$: C 78.66, H 6.05, N 15.29; found: C 78.19, H 6.25, N 15.14.

The mass spectrum of **19** showed no contamination by undesired phthalocyanines. As a comparison, an attempt was made to purify the same crude **19** by a series of four ordinary flash chromatographic operations. The mass spectrum of its purest part showed that it still contained some 2,9,16,23-tetra-*tert*-butylphthalocyanine.

2-*tert*-Butyl-9,16,23-tri-*n*-pentoxophthalocyanine (20)

A solution of **16** derived from 107 mg (0.5 mmol) of 4-*n*-pentoxophthalonitrile (**28**) and **17** derived from 276 mg (1.5 mmol) of 4-*tert*-butylphthalonitrile (**27**) in 2 mL of 2-*N,N*-dimethylaminoethanol was heated under reflux for 48 h. The dark blue mixture was then poured into 50 mL of distilled water to form a precipitate. The precipitate was filtered and washed with methanol for a few times until the filtrate was colourless. After column chromatography with flash silica gel as the static phase and toluene as the eluting solvent, 115 mg of a phthalocyanine mixture was obtained, in about 28% yield, as a purple solid. The phthalocyanine mixture was then subjected to both ordinary flash chromatography and chromatography using Pc-Si-Gels **9** or **14** with carbon tetrachloride/toluene (70/30–0/100) as the eluting solvent. Reverse phase HPLC was used as the monitor to check the purity of the eluted fractions. After six repetitive chromatographic separations and precipitation from methanol, 10.5 mg of the desired 2-*tert*-butyl-9,16,23-tri-*n*-pentoxophthalocyanine (**20**) was obtained, in 2.5% yield, as a purple solid; IR (KBr, cm^{-1}): 3300 (w, NH), 1620 (vs, C=C), 1240 (s, COC), 1100 (s, COC), 1020 (vs, NH); 750 (s, CH_{arom}); UV–VIS (1,2-dichlorobenzene, nm) (log ϵ): 708 (5.20), 674 (5.11), 640 (4.66), 607 (4.47), 348 (4.85); ^1H nmr (CDCl_3) δ : 7.3–9.7 (vbr, aromatic), 4.1–4.6 (m, $-\text{OCH}_2\text{C}-$, 6H), 1.1–1.6 (m, $-\text{CH}_3$, 36H), -3.5 (br N-H); ^{13}C nmr (toluene- d_8) δ : 118–160 (C_{arom}), 78 (CH_2O), 27.2 ($\text{C}-\text{CH}_3$), 19.7–21.2 ($\text{C}-\text{CH}_3$); MS (FAB) m/z : 829 ($\text{M}^+ + 1$, 100%), 759 (20%). Anal. calcd. for $\text{C}_{51}\text{H}_{50}\text{N}_8\text{O}_3$: C 73.89, H 6.81, N 13.52; found: C 73.98, H 6.84, N 13.12.

2,3-Di-(1-Octyn-1-yl)-9,16,23-trimethoxymethoxyphthalocyaninato zinc(II) (23)

A mixture of **21** (425 mg, 1.24 mmol) (**19**), **22** (467 mg, 2.48 mmol) (**19**), DBU (2 mL), and 1-butanol (4 mL) was heated under reflux with stirring in an argon atmosphere. After 5–10 min, 184 mg (1.0 mmol) of dry zinc acetate was added. After heating for 4–5 h, the dark green-blue mixture was poured into 400 mL of water, and then extracted three times with toluene. The organic phase was washed with water until it was neutral, then dried with magnesium sulphate. After filtration and evaporation, the crude product underwent a preliminary silica flash column chromatography with toluene/ethyl acetate (50/50–0/100) as the eluting solvent. A mixture of phthalocyanines (320 mg) was obtained in about 40% yield, and reverse phase HPLC showed it contained about 40% of the desired phthalocyanine **23**. After three more separations by flash column chromatography with toluene/ethyl acetate (92/8–86/14) as the eluting solvent, 100 mg of the desired 2,3-diocetyl-9,16,23-trimethoxymethoxyphthalocyaninato zinc(II) (**23**) was obtained, as a purple solid, in 12.4% yield with **22** as the limiting reactant; IR (KBr, cm^{-1}): 1620 (vs, C=C), 1240 (s, COC), 1100 (s, COC), 750 (s, CH_{arom}); UV–VIS (1,2-dichlorobenzene, nm) (log ϵ): 698 (5.12), 682 (5.02), 624 (4.39), 357 (4.80); ^1H nmr (Benzene- d_6) δ : 6.94–8.81 (vbr, aromatic, 11H), 4.73–5.02 (m, $-\text{OCH}_2\text{O}-$, 6H), 2.97–3.16 (m, CH_3O , 9H), 2.57–2.70 (m, $\text{C}\equiv\text{C}-\text{CH}_2-$, 4H), 1.07–1.87 (m, $-\text{C}-\text{CH}_2\text{C}-$, 16 H), 0.54–0.64 (tri, CH_2CH_3 , 6H); MS (FAB) m/z : 972 (M^+ , 100%), 928 (85%), 888 (50%). Anal. calcd. for $\text{C}_{54}\text{H}_{52}\text{N}_8\text{O}_8\text{Zn}$: C 66.56, H 5.38, N 11.50, Zn 6.71; found: C 65.81, H 5.14, N 11.12, Zn 6.64.

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