The syntheses of 2,9,16,23- and 1,8,15,22-tetrahydroxyphthalocyanines

CLIFFORD C. LEZNOFF,[1] MOUGANG HU, COLIN R. MCARTHUR, AND YONGNIAN QIN
Department of Chemistry, York University, North York (Toronto), ON M3J 1P3, Canada

AND

JOHAN E. VAN LIER
Medical Research Council Group in the Radiation Sciences, Faculty of Medicine, University of Sherbrooke, Sherbrooke, QC J1H 5M4, Canada

CLIFFORD C. LEZNOFF, MOUGANG HU, COLIN R. MCARTHUR, YONGNIAN QIN, and JOHAN E. VAN LIER. Can. J. Chem. **72**, 1990 (1994).

2,9,16,23-Tetra-*p*-*n*-butylbenzyloxy-, 2,9,16,23-tetradiphenylmethoxy-, 2,9,16,23-tetramethoxymethoxy-, and 1,8,15,22-tetra-*p*-*n*-butylbenzyloxyphthalocyanines were synthesized from the appropriate phthalonitriles. Metal-free phthalocyanines were converted to their zinc derivatives. Cleavage from the appropriate precursor with trifluoroacetic acid produced 2,9,16,23-tetrahydroxyphthalocyanine and 1,8,15,22-tetrahydroxyphthalocyanine and their zinc derivatives. NMR spectroscopy revealed that all the 2,9,16,23-tetrasubstituted phthalocyanines are the usual mixtures of the 2,9,16,23, 2,9,16,24, 2,9,17,24, and 2,10,16,24 isomers, but the two 1,8,15,22-tetrasubstituted phthalocyanines were formed as *pure single isomers*.

CLIFFORD C. LEZNOFF, MOUGANG HU, COLIN R. MCARTHUR, YONGNIAN QIN et JOHAN E. VAN LIER. Can. J. Chem. **72**, 1990 (1994).

Utilisant les phtalonitriles appropriés comme produits de départ, on a synthétisé les 2,9,16,23-tétra-*p*-*n*-butylbenzyloxy-, 2,9,16,23-tétraphénylméthoxy-, 2,9,16,23-tétraméthoxyméthoxy- et 1,8,15,22-tétra-*p*-*n*-butylbenzyloxyphtalocyanines. On a transformé les phtalocyanines libres de métal en dérivés zinciques. Le clivage du précurseur approprié avec de l'acide trifluoroacétique conduit à la 2,9,16,23-tétrahydroxyphtalocyanine et à la 1,8,15,22-tétrahydroxyphtalocyanine et à leurs dérivés zinciques. La RMN révèle que toutes les phtalocyanines tétrasubstituées en 2,9,16,23 sont formées des mélanges habituels des isomères 2,9,16,23, 2,9,16,24, 2,9,17,24 et 2,10,16,24; toutefois, les deux phtalocyanines substituées en 1,8,15,22 sont des *isomères purs*.

[Traduit par la rédaction]

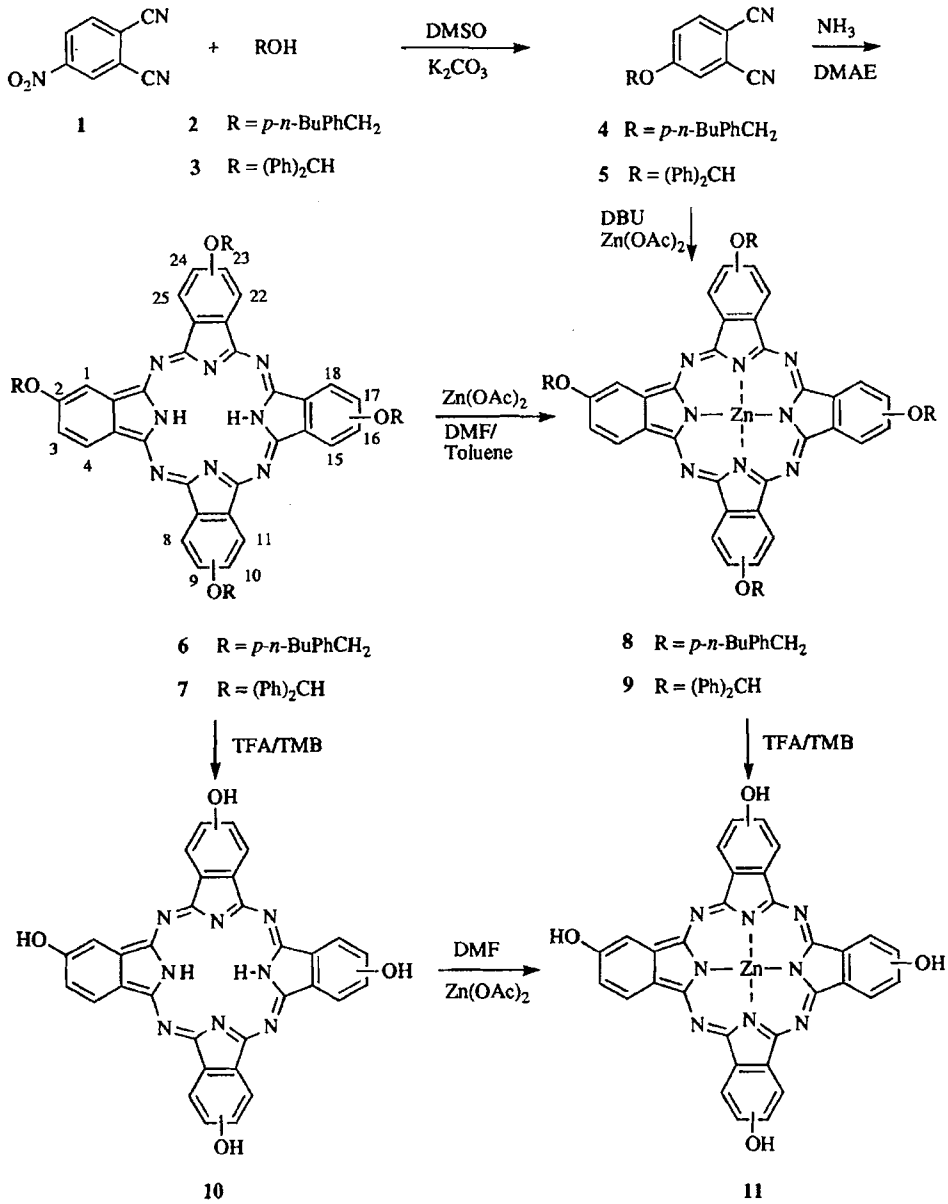
Introduction

The first synthesis of 2,9,16,23-tetrahydroxyphthalocyanine was reported in 1987 (1) and its phototoxicity in the photodynamic therapy (PDT) of cancer tumours (2–5) investigated (1, 6–8). Previously, it was shown that changes in the length of the spacer group (8) on hydroxyphthalocyanine affected the phototoxicity and in this study we also wished to show variation in the *position* of the hydroxy group on the phthalocyanine ring. The above compound was prepared by the boron tribromide cleavage of 2,9,16,23-tetraneopentoxyphthalocyanine, as the desired synthesis from a hydroxyphthalonitrile only resulted in decomposition of the starting material (1). Although the preparation was basically successful, the reaction conditions were quite critical and the yields were sometimes inadequate because of the incomplete cleavage of the substituted phthalocyanine precursor and the slow decomposition of the tetrahydroxyphthalocyanine under the attempted reaction conditions. In addition, purification of 2,9,16,23-tetrahydroxyphthalocyanine was performed on a silica gel column and the tetrahydroxyphthalocyanine either decomposes on silica gel or is poorly recovered from that media. For example, when a small-scale sample (50 mg) of 2,9,16,23-tetrahydroxyphthalocyananine was purified, the recovery achieved was only 53%, while on a larger scale (1.26 g), the recovery from the column was only 22% (1). Thus, new synthetic and purification methods need to be discovered for the preparation of tetrahydroxyphthalocyanines. Since 2,9,16,23-tetrahydroxyphthalocyanine was originally obtained as a mixture of related isomers, the development of new methods to easily prepare other polyhydroxyphthalocyanines, these mixtures or, more desirably, pure single isomers for PDT were sought.

Benzyl (9), diphenylmethyl (10), and trityl (11) groups are often used to protect phenolic and hydroxy groups (12). These protecting groups are more easily removed than neopentyl moieties to give free phenolic-type functional groups using different methods (13). The methoxymethyl ether moiety (MOM) (or its analogs) is also a useful protecting group for phenols (14). We examined the possibility of preparing tetrahydroxyphthalocyanines by using different kinds of reagents to deprotect the hydroxy blocking groups of the substituted phthalocyanines. In addition, a new procedure was developed to purify tetrahydroxyphthalocyanine.

Identically tetrasubstituted phthalocyanines are almost always synthesized as mixtures of statistical isomers consisting of the 2,9,16,23, 2,9,16,24, 2,9,17,24, and 2,10,16,24 isomers, and very few studies have been directed toward the exclusive formation of one isomer of a tetrasubstituted phthalocyanine (15). Although the 2,9,16,23-tetraneopentoxyphthalocyaninato zinc(II) (16) and 2,9,17,24-tetra-*tert*-butylphthalocyaninato zinc(II) (17) were produced as pure isomers, several reaction steps were used and only low yields were obtained. The synthesis of a single isomer of 1,2-naphthalocyanine has been achieved (18) due to the steric constraints of the benzo substituents, but other 1,8,15,22-tetrasubstituted phthalocyanines gave mixtures of isomers that in one example could be separated by high performance liquid chromatography (HPLC) (19). In this paper we report the exclusive synthesis of two 1,8,15,22-tetrasubstituted phthalocyanines and their zinc derivatives as pure single isomers in high yields under common conditions. We examined the ^{1}H NMR and ^{13}C NMR spectra of these pure compounds and compared these spectra with those of the phthalocy-

[1]Author to whom correspondence may be addressed.



SCHEME 1

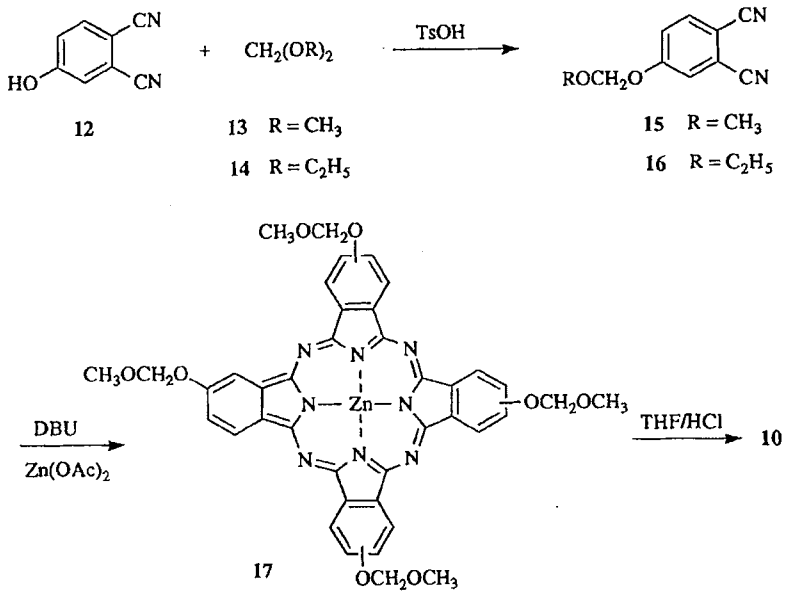
anines produced as mixtures of statistical isomers. Analyses of these spectra revealed that all the 2,9,16,23-tetrasubstituted phthalocyanines were indeed mixtures of isomers (for convenience numbered as the 2,9,16,23 derivatives only) but that the 1,8,15,22-tetrasubstituted phthalocyanines were produced as *pure single compounds*.

Results and discussion

The preparation of 2,9,16,23-tetrasubstituted phthalocyanines as mixtures of isomers

Using a new procedure developed in our laboratory (20, cf. ref. 21), 4-nitrophthalonitrile (**1**) reacted with *p-n*-butylbenzyl alcohol (**2**) or diphenylmethanol (**3**) in dimethyl sulfoxide (DMSO) at room temperature to give 4-*p-n*-butylbenzyloxyphthalonitrile (**4**) or 4-diphenylmethoxyphthalonitrile (**5**) in 90 or 92% yield, respectively (Scheme 1). The self-condensation of **4** or **5** in dimethylaminoethanol gave 2,9,16,23-tetra(*p-n*-butylbenzyloxy)phthalocyanine (**6**) or 2,9,16,23-tetra(diphenylmethoxy)phthalocyanine (**7**) in 17 or 25% yield, respectively. Refluxing the metal-free phthalocyanines (Pcs) **6** or **7** with zinc acetate in DMF and toluene gave 2,9,16,23-tetra(*p-n*-butylbenzyloxy)phthalocyaninato zinc(II) (**8**) or 2,9,16,23-tetra(diphenylmethoxy)phthalocyaninato zinc(II) (**9**), both in 90% yield. The zinc derivatives **8** and **9** could be prepared directly from **4** and **5**, respectively (22), in an improved procedure. Thus **4** or **5** reacted at 100°C with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (23) as a base and zinc acetate as a template during which ammonia gas was introduced into the reaction. Using this one-step improved procedure, **4** and **5** were produced in overall yields of 65 and 70%, respectively (Scheme 1).

Although catalytic hydrogenation (24), catalytic transfer hydrogenation (25), iodotrimethylsilane and chlorotrimethylsilane (26) couldn't efficiently cleave the alkyoxyphthalocyananines **6** and **7**, cleavage of the metal-free protected Pcs under reflux conditions with trifluoroacetic acid (TFA) (27) in the



SCHEME 2

presence of a polyalkylbenzene (1,2,4,5-tetramethylbenzene (TMB) in this instance) as a benzyl cation scavenger (28) gave the desired 2,9,16,23-tetrahydroxyphthalocyanine (**10**) in 60–70% yield. Similarly, cleavage for 5 h of the protected zinc Pcs **8** or **9** gave 2,9,16,23-tetrahydroxyphthalocyaninato zinc(II) (**11**) in 84–88% yield. Alternatively, metal-free **10** can be metallated with zinc acetate in DMF–toluene as for **8** to give the zinc Pc **11**. The poor solubility of **10** contributes to the fact that **11** is more easily prepared via **8** or **9** (Scheme 1).

Phenols are usually converted to trityl or methoxymethyl (MOM) ethers by treatment with base and trityl chloride or methoxymethyl chloride. Since 4-hydroxyphthalonitrile (**12**) is unable to react with trityl chloride to give the corresponding ether and is unstable to basic conditions, **12** was treated with dimethoxymethane (**13**) or diethoxymethane (**14**) under acidic conditions (29) to give 4-methoxymethoxyphthalonitrile (**15**) and 4-ethoxymethoxyphthalonitrile (**16**) in 92 and 95% yield, respectively. 2,9,16,23-Tetra(methoxymethoxy)phthalocyaninato zinc(II) (**17**) was prepared from **15** in 30% yield in a previous procedure (23), but similar treatment of **16** gave mostly decomposition products. When the improved procedure as described for **8** and **9** was used, compound **17** was prepared in 60% yield. Treatment of **17** with HCl–THF under reflux conditions gave **10** in 31% yield (Scheme 2). The acidic cleavage conditions resulted in demeltallation of the zinc Pc so that **10** and not **11** was isolated.

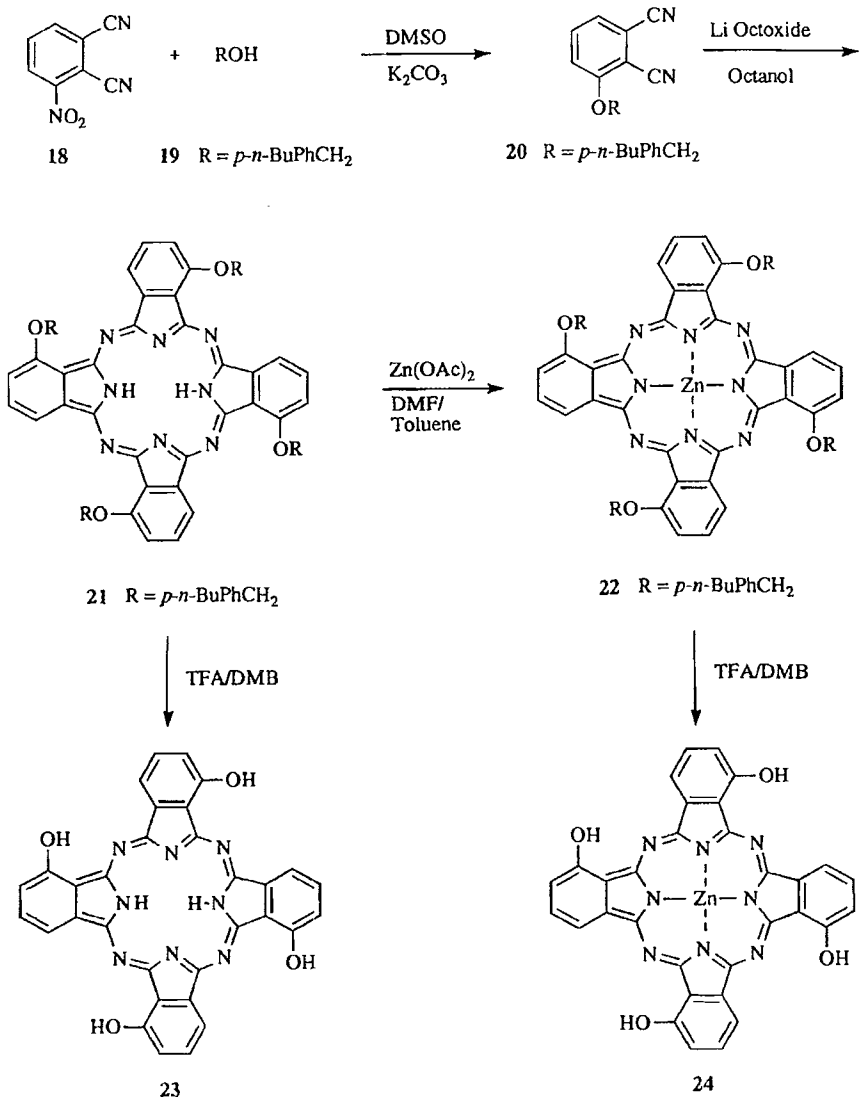
Although classical chromatography on silica gel is not suitable for the purification of tetrahydroxyphthalocyanines because of either decomposition on silica gel or poor recovery from that media, gel permeation chromatography resolved this problem and **10** and **11** were readily purified by this latter method.

The preparation of 1,8,15,22-tetrahydroxyphthalocyanine as a pure single isomer

3-Nitrophthalonitrile (**18**) reacted with *p-n*-butylbenzyl alcohol (**2**) as for **4** and **5** to give 3-*p-n*-butylbenzyloxyphthalonitrile (**20**) in 95% yield. The usual procedures for preparation of 2,9,16,23-tetrasubstituted phthalocyanines did not subsequently give 1,8,15,22-tetra(*p-n*-butylbenzyloxy)phthalocyanine (**21**) and its zinc derivative (**22**). Phthalocyanines **21** and **22** could be prepared by heating **20** in a solution of lithium octoxide in *n*-octanol (Scheme 3). Quenching the reaction mixture with water and methanol gave the metal-free phthalocyanine **21** in 40% yield. When zinc acetate was added to the reaction mixture at 100°C and the temperature was controlled below or at 100°C, the zinc derivative **22** of the metal-free phthalocyanine could be obtained in 80% yield. 1,8,15,22-Tetrahydroxyphthalocyanine (**23**) and its zinc derivative (**24**) can be prepared as above by cleavage of **21** and **22** with TFA and TMB in 25 and 85% yield, respectively. Pc **22** can easily be prepared from Pc **21** by refluxing it with zinc acetate in DMF–toluene in 85% yield.

Spectroscopic and physical properties

NMR spectroscopy of 2,9,16,23-tetrasubstituted phthalocyanines generally exhibits broad absorptions in the aromatic and other spectral regions due to the presence of four isomers, but occasionally the resonances can be resolved (15, 30). Similarly, 1,8,15,22-tetrasubstituted phthalocyananines or analogs can exist as a distribution of four isomers (15, 31) but in this substitution pattern steric effects can afford a nonstatistical distribution of the four products. More recently, Hanack et al. actually separated all four isomers of 1,8,15,22-, 1,11,15,25-, 1,8,18,22-, and 1,8,15,25-tetrasubstituted phthalocyanines (19). In contrast, in our research, the 1,8,15,22-tetra(*p-n*-butylbenzyloxy)phthalocyanine (**21**) and its zinc derivative (**22**) were produced *exclusively*, presumably due to the greater steric constraints of the *p-n*-butylbenzyloxy substituent. ^{1}H NMR spectra of this phthalocyanine (**21**) and its zinc derivative (**22**) (Fig. 1) show doublet, triplet, and doublet absorbance peaks for protons of the phthalocyanine ring in the downfield region, and only one single peak at 5.9 ppm for protons of the -OCH_2- of the benzyl group in **21** and at 6.3 ppm for protons of the -OCH_2 of the benzyl group in **22** (Fig. 1). The ^{1}H NMR spectrum of 1,8,15,22-tetrahydroxyphthalocyaninato zinc(II) (**24**) (Fig. 1) shows a singlet at 10.56 ppm (phenol group), a doublet at 8.58–8.56, a triplet at 8.28–8.22, and a doublet at 7.83–7.81 ppm for



SCHEME 3

the three other protons attached to the phthalocyanine ring, while 2,9,16,23-tetrahydroxyphthalocyaninato zinc(II) (**11**) and its precursor **8** and its isomers show multiplets at 10.65–10.63 ppm (phenol group), 9.19–9.15, 8.70–8.68, and 7.67–7.63 ppm for the other three protons (Fig. 1). The *J*-modulated spin echo (JMOD) ^{13}C NMR spectrum of compound **22** shows only singlet NMR absorbance peaks for those identical carbons that make up the Pc ring. Thus, the NMR spectra support the conclusion that **21–24** exist as single isomers.

Some other physical properties of **21–24**, such as the formation of crystals and their relatively low solubility, support this conclusion. In general, tetrasubstituted Pcs are polymorphic solids due to the presence of statistically produced isomers, 1,8,15,22-Tetra-(*p*-*n*-butylbenzyloxy)phthalocyaninato zinc(II) (**22**) was directly produced as crystalline needles while recrystallization from THF gave square crystals. The solubilities of **21–24** are informative. For example, 2,9,16,23-tetra-(*p*-*n*-butylbenzyloxy)phthalocyanine (**6**) is very soluble in many organic solvents such as dichloromethane, chloroform, DMF, THF, and ethyl acetate, but 1,8,15,22-tetra-(*p*-*n*-butylbenzyloxy)phthalocyanine, its constitutional isomer, does not dissolve in most solvents and only slightly in THF and pyridine. The UV–visible spectra of **21–24** contrast strongly with those of **6**, **8**, **10**, and **11**. For example, **24** exhibits a strong *Q*-band at 719 nm compared to **10** at 684 nm (1, 32). Although tetrahydroxyphthalocyanines cannot be made directly from hydroxyphthalonitriles, the use of appropriate blocking groups can lead to their syntheses both as mixtures of isomers or, in the case of **23** or **24**, as pure single isomers.

Experimental

Matheson high-purity argon was used to maintain inert atmosphere conditions. Thin-layer chromatography (TLC) was performed using silica gel G as the adsorbent. Flash chromatography was performed using silica gel of particle size 20–45 μm. Gel permeation chromatography was performed using Bio-beads, SX-2, 200–400 mesh. Melting points (mp) were determined using a Kofler hot stage melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Pye Unicam SP1000 infrared spectrophotometer using KBr disks. Nuclear magnetic resonance (NMR) spectra for protons and carbons were recorded on a Bruker AM300 NMR spectrometer. The positions of signals are reported in δ units. (The splitting of the signal is described as singlets (s), doublets (d), triplets (t), quartets (q), doublets

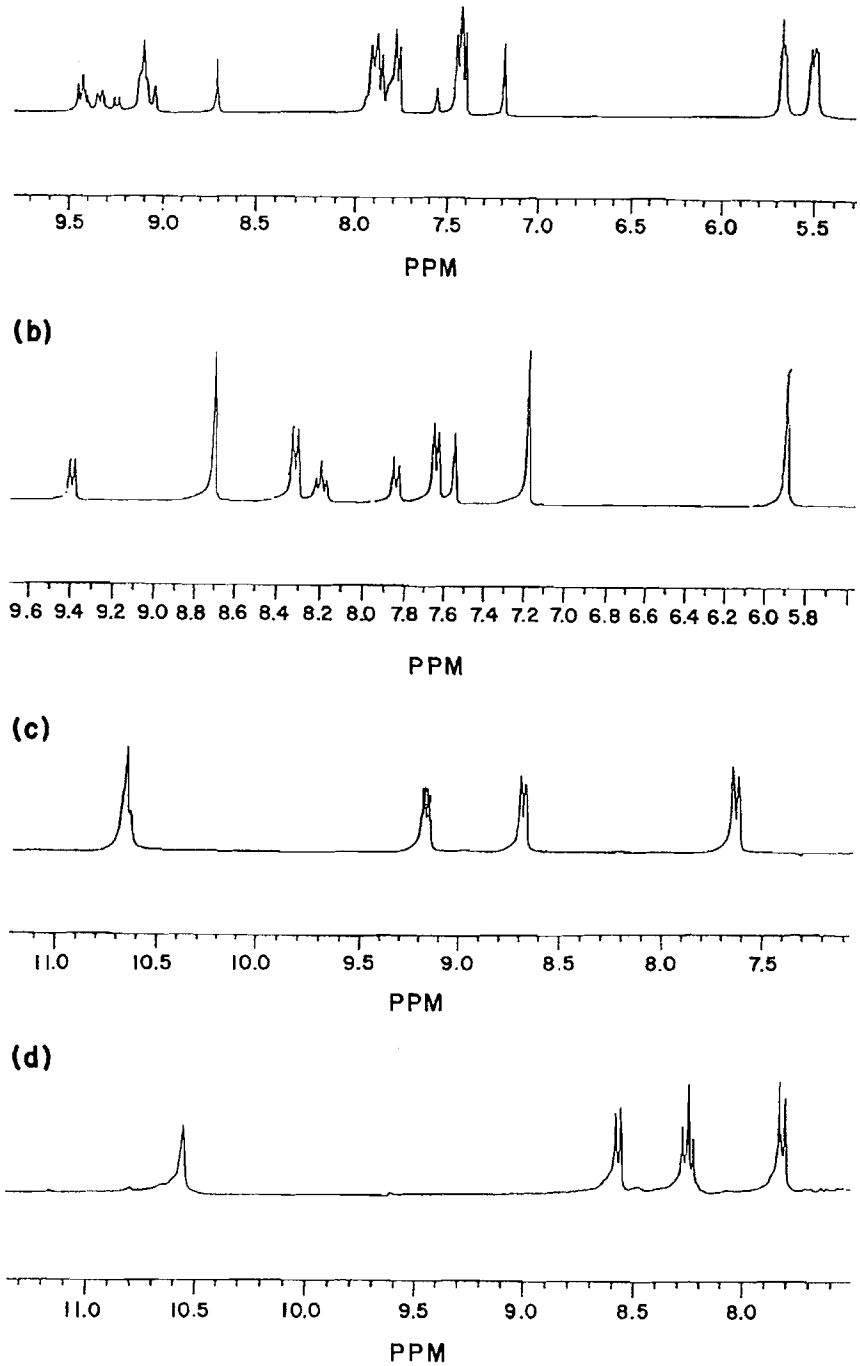


FIG. 1. The ^{1}H nmr spectra of tetrasubstituted phthalocyaninato zinc(II) compounds in pyridine-d_5 (*a*, *b*) and DMSO-d_6 (*c*, *d*); (*a*) 2,9,16,23-tetra(*p*-*n*-butylbenxyloxy)phthalocyaninato zinc(II) (**8**); (*b*) 1,8,15,22-tetra(*p*-*n*-butylbenzyloxy)phthalocyaninato zinc(II) (**22**); (*c*) 2,9,16,23-tetrahydroxyphthalocyaninato zinc(II) (**11**); (*d*) 1,8,15,22-tetrahydroxyphthalocyaninato zinc(II) (**24**); *: peaks of solvent.

of doublets (dd), or multiplets (m).) The ultraviolet–visible spectra (UV) 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. The FAB spectra were obtained with a Kratos MS-50 triple analyzer mass spectrometer equipped with a FAB ion source of standard Kratos design and Ion Tech atom gun. Microanalyses were performed by Guelph Chemical Laboratories Ltd., Guelph, Ontario.

*4-*p-n-*Butylbenzyloxyphthalonitrile (4)*

Method I (21)

To a solution of 0.52 g (3.0 mmol) of 4-nitrophthalonitrile (**1**) in 10 mL of dimethylformamide (DMF) was added 0.41 g (2.5 mmol) of *p*-*n*-butylbenzyl alcohol (**2**) and 1.05 g (7.5 mmol) of finely ground potassium carbonate. This reaction mixture was stirred at room temperature for 96 h and poured into 30 mL of ice-water to give a yellow precipitate. The precipitate was collected by filtration, washed with cold water, and dried, The crude product was purified by column chromatography on silica gel, using THF–hexane (15:85) as eluant. Evaporation of the solvent gave a pale-yellow solid. Recrystallization of the solid in THF–hexane 3:7 gave 0.54 g (75%) of **4** as white crystals.

Method II

A improved method was used to prepare **4**. To a solution of 0.52 g

(3.0 mmol) of **1** in 10 mL of dimethyl sulfoxide (DMSO) was added 0.41 g (2.5 mmol) of **2** and 0.25 g (1.88 mmol) of finely ground potassium carbonate. The mixture was stirred for 96 h. Then another three 0.25-g portions of potassium carbonate were added to the mixture in 20-h intervals and the mixture was pumped under vacuum (20) for 5 min in 10-h intervals during the reaction. Ice-water (30 mL) was added with stirring to the mixture. The precipitate was collected by filtration, washed with cold water, and dried. After column chromatography on silica gel and recrystallization in THF and hexane (3:7), 0.65 g of a white crystalline material **4** was obtained in 90% yield, mp 64.5–65.5°C; IR (KBr, cm^{-1}): 3095, 3040, 2960, 2930, 2860, 2230 (CN), 1590, 1490, 1320, 1250, 1085, 990, 875, 845; ^1H NMR ($CDCl_3$) δ: 7.71–7.68 (d, $J = 4$ Hz, 1H), 7.32–7.21 (m, 6H), 5.11 (s, 2H), 2.65–2.60 (t, $J = 15$ Hz, 2H), 1.65–1.55 (m, 2H), 1.42–1.33 (m, 2H), 0.95–0.90 (t, $J = 15$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ: 161.89, 143.82, 135.20, 131.78, 128.97, 127.71, 120.09, 119.80, 117.44, 115.69, 107.43, 71.14, 35.37, 33.50, 22.34, 13.90; MS for ($C_{19}H_{18}N_2O$), *m/z* (relative intensity): 291 ($(M + 1)^+$, 18), 247 (19), 147 ($(C_4H_9PhCH_2)^+$, 100), 127 (24), 116 (35), 104 (47), 91 (41), 78 (30), 64 (27), 51 (25). Anal. calcd. for $C_{19}H_{18}N_2O$: 78.59, H 6.25, N 9.65; found: C 78.21, H, 6.47, N 9.50.

4-Diphenylmethoxyphthalonitrile (5)

A procedure previously described for the preparation of **4** (Method II) was used to prepare **5** in 92% yield as white crystals, mp 156–157°C; IR (KBr, cm^{-1}) 3080, 3020, 2950, 2920, 2848, 2230, 2220, 1575, 1468, 1295, 1180, 1040, 820, 790; ^1H NMR ($CDCl_3$) δ: 7.92–7.89 (d, $J = 9$ Hz, 1H), 7.70–7.68 (d, $J = 2.5$ Hz, 6H), 7.55–7.57 (m, 5H), 7.40–7.29 (m, 6H), 6.78 (s, 1H); ^{13}C NMR ($CDCl_3$) δ: 161.09, 139.00, 135.15, 129.05, 128.64, 126.74, 121.14, 120.68, 117.44, 115.54, 115.17, 107.71, 83.16; MS for $C_{21}H_{14}N_2O$, *m/z* (relative intensity): 310 (M^+, 6%), 285 (48), 237 (32), 167 (Ph_2CH^+, 100), 152 (58), 115 (54), 89 (50), 82 (73), 63 (32), 51 (16). Anal. calcd. for $C_{21}H_{14}N_2O$: C 81.27, H 4.55, N 9.03; found: C 81.50, H 4.48, N 9.21.

*2,9,16,23-Tetra(*p-n-*butylbenzyloxy)phthalocyanine (6)*

Compound **4** (0.405 g, 1.4 mmol) was suspended in 5 mL of 2-dimethylaminoethanol (DME). The suspension was heated to 80°C and the phthalonitrile dissolved. A steady stream of ammonia gas was introduced into the solution for 2 h. The temperature was raised to reflux and maintained, along with ammonia introduction, for 10 h. The mixture was cooled to room temperature and centrifuged to give a blue solid. The solid was washed with hexane and methanol. Further purification was performed on a flash silica gel column, eluting with THF and hexane (2:8). Evaporation of the solvent gave 0.069 g (17%) of a shining blue solid, mp >320°C; UV–vis (THF) λ_{max} (log ε): 702 (5.00), 666 (4.97), 638 (4.72), 608 (3.60); IR (KBr, cm^{-1}): 3300 (N-H), 3040, 3020, 2960, 2940, 2862, 1614, 1505, 1480, 1460, 1380, 1320, 1250, 1120, 1100, 1015, 940, 825, 750; ^1H NMR ($CDCl_3$) δ: 7.79–6.95 (m, br, 28H), 4.81–4.70 (m, br, 8H), 2.82–2.68 (t, 8H), 1.69–1.58 (p, 8H), 1.37–1.22 (m, 8H), 1.05–1.01 (t, 12H), −5.95 (s, br, 2H); MS (FAB) for $C_{76}H_{74}O_4$, *m/z* (relative intensity): 1164 ($(M + 2)^+$, 48), 1017 {$((M + 2)680 - R)^+$, 39}, 870 {$((M + 2)680 - 2R)^+$, 56}, 724 {$((M + 2\ 680 - 3R)^+$, 85}, 580 ($(M - 4R)^+$, 79. Anal. calcd. for $C_{79}H_{74}N_8O_4$: C 78.46, H 6.41, N 9.63; found: C 78.79, H 6.60, N 9.45.

2,9,16,23-Tetra(diphenylmethoxy)phthalocyanine (7)

A method previously described for the preparation of **6** was used to prepare **7**. After collection by centrifugation and washing, the crude product was applied onto a flash silica gel column and eluted with toluene. Evaporation of the solvent gave a shining, blue solid in 25% yield, mp >320°C; UV–vis (THF) λ_{max} (log ε): 704 (471), 668 (4.64), 641 (4.20), 605 (4.02), 390 (4.13), 351 (4.34); IR (KBr, cm^{-1}): 3300 (N-H), 3030, 3010, 2820, 1690, 1610, 1500, 1480, 1460, 1400, 1350, 1325, 1235, 1120, 1100, 1020, 750, 700; ^1H NMR ($CDCl_3$) δ: 8.38–808 (m), 7.99–7.80 (m), 7.77–7.29 (m), 7.20–7.10 (m), 6.80–6.71 (m, 8H), −3.92 (b, 2H); MS (FAB) for $C_{85}H_{58}N_8O_4$, *m/z* (relative intensity): 1243 ($(M + 1)^+$, 13), 1076 {$((M + 1)680 - 2R)^+$, 55}, 742 {$((M + 1)680 - 3R)^+$, 65}, 576 {$((M + 1)680 - 4R)^+$, 100}. Anal. calcd. for $C_{84}H_{58}N_8O_4$: C 81.14, H 4.66, N 9.01; found: C 81.21, H 4.03, N 9.15.

*2,9,16,23-Tetra(*p-n-*butylbenzyloxy)phthalocyaninato zinc(II) (8)*

Method I

Compound **4** (0.81 g, 2.8 mmol) was suspended in 10 mL of DME. The suspension was heated to 100°C and a steady stream of ammonia gas passed into the solution for 2 h. To the solution was added 1.5 mL of 1,8-diazatricyclo[5.4.0]undec-7-ene (DBU) followed by 546 mg (3.0 mmol) of zinc acetate after 0.25 h. The introduction of ammonia was continued for 10 h at 100–115°C. The mixture was cooled to room temperature and 30 mL of methanol and water (1:1) was added. The precipitate was collected by centrifugation, and washed with water, methanol, and hexane. Further purification was performed in a flash silica gel column by eluting with THF and hexane (2:8). Evaporation of the solvent gave 0.557 g of a shining, blue solid in 65% yield.

Method II

Compound **8** could also be prepared from **6**. To 116 mg (0.1 mmol) of **6** in 5 mL of toluene and DMF (1:1) was added 91 mg (0.4 mmol) of zinc acetate. The mixture was refluxed for 24 h. The mixture was cooled to room temperature and 10 mL of methanol and water (1:1) was added. The precipitate was collected by centrifugation, and washed with water, methanol, and hexane. The solid was put onto a flash silica gel column and eluted with THF and hexane (3:7). Evaporation of the solvent gave 110 mg (90% yield) of a shining, blue solid as pure **8**, mp >320°C; UV–vis (THF) λ_{max} (log ε): 682 (5.34), 610 (4.41), 350 (4.89); IR (KBr, cm^{-1}): 3040, 3010, 2950, 2930, 2860, 1910, 1735, 1705, 1580, 1532, 1450, 1400, 1325, 1250, 1160, 1100, 1030, 950, 850; ^1H NMR (pyridine-d_5) δ: 9.45–9.05 (m, 8H), 7.95–7.77 (m, 12H), 7.46–7.19 (m, 8H), 5.67–5.49 (m, 8H), 2.67–2.63 (t, 8H), 1.66–1.57 (p, 8H), 1.40–1.28 (m, 8H), 0.93–0.88 (t, 12H); JMOD ^{13}C NMR (pyridine-d_5) δ: 161.41–161.16 (m, 1 × 4C), 153.80–152.84 (m, 2 × 4C), 143.16–143.12 (d, 1 × 4C), 141.30–141.03 (m, 1 × 4C); 135.11–135.08 (d, 1 × 4C), 132.47–132.20 (m, 1 × 4C), 129.22–129.15 (d, 2 × 4C), 128.67–128.59 (d, 2 × 4C), 124.17 (m, b, 1 × 4C), 118.53 (m, b, 1 × 4C), 106.98 (m, b, 1 × 4C), 71.09 (s, 4C), 35.65 (s, 4C), 33.92 (s, 4C), 22.65 (s, 4C), 14.12 (s, 4C); MS (FAB) for $C_{76}H_{72}N_8O_4Zn$, *m/z* (relative intensity): 1226 ($(M + 2)^+$, 62), 1079 {$((M + 2)680 - R)^+$, 63}, 932 {$((M + 2)680 - 2R)^+$, 57}, 785 {$((M + 2)680 - 3R)^+$, 67}, 638 {$((M + 2)680 - 4R)^+$, 100}. Anal. calcd. for $C_{76}H_{72}N_8O_4Zn$: C 74.41, H 5.92, N 9.13; found: C 74.00, H 5.80, N 8.82.

2,9,16,23-Tetra(diphenylmethoxy)phthalocyaninato zinc(II) (9)

The methods (Method I and Method II) previously described for the preparation of **8** were used to prepare **9** in 70 and 90% yield, respectively, as a shining, blue solid, mp >320°C; UV–vis (THF) λ_{max} (log ε): 679 (5.74), 611 (4.71), 351 (5.31); IR (KBr, cm^{-1}): 3030, 3010, 2870, 1610, 1530, 1450, 1380, 1325, 1250, 1210, 1155, 1100, 1025, 845, 785; ^1H NMR (pyridine-d_5) δ: 9.55–9.50 (m, 8H), 8.72–8.07 (m, 4H), 7.94–7.69 (m, 16H), 7.52–7.37 (m, 28H); ^{13}C NMR (pyridine-d_5) δ: 160.68–160.46 (m, 1 × 4C), 154.91–153.15 (m, 2 × 4C), 142.29 (s, 2 × 4C), 141.16–140.9 (m, 1 × 4C), 132.77–132.64 (m, 1 × 4C), 129.26 (s, 4 × 4C), 128.32 (s, 2 × 4C), 127.64 (s, 4 × 4C), 124.44 (m, 1 × 4C), 119.48–119.39 (m, 1 × 4C), 109.50 (m, 1 × 4C), 82.57 (s, 1 × 4C); MS (FAB) for $C_{85}H_{56}N_8O_4Zn$, *m/z* (relative intensity): 1305 ($(M + 1)^+$, 100), 1139 {$((M + 2)680 - R)^+$, 62}, 972 {$((M + 2)680 - 2R)^+$, 33}, 805 {$((M + 2)680 - 3R)^+$, 20}, 638 {$((M + 2)680 - 4R)^+$, 18}. Anal. calcd. for $C_{84}H_{56}N_8O_4Zn$: C 77.21, H 4.32, N 8.58; found: C 76.88, H 3.85, N 8.70.

2,9,16,23-Tetrahydroxyphthalocyanine (10) (1)

To 60 mg (0.052 mmol) of **6** in 5 mL of trifluoroacetic acid (TFA) was added 27.9 mg (0.208 mmol) of 1,2,4,5-tetramethylbenzene (TMB). The mixture was refluxed for 15 h. The TFA was evaporated and the residue was washed with hexane. The residue was dissolved in THF and the solution was put onto a gel permeation column, eluting with THF. Evaporation of the solvent gave 18 mg (60%) of **10** as a green solid. When **7** was used to prepare **10**, the reaction time was 10 h and the yield was 70%; UV–vis (2-methoxyethanol) λ_{max} (log ε): 708 (4.89), 672 (4.85), 639 (4.53), 614 (4.32), 390 (4.40), 342 (4.72), 292 (4.54), 232 (4.45); IR (KBr, cm^{-1}): 3100–3500 (phenolic group), 1610,

1480, 1310, 1200, 1250, 1095, 1010, 930, 820, 740, 710; ^{1}H NMR (DMSO-d_6) δ: 10.45 (br, 4H (phenolic group)), 8.48 (m, 4H), 8.10 (m, 4H), 7.43 (br, 4H), −3.10 (br, 2H); MS (FAB) for $C_{32}H_{18}N_8O_4$, *m/z* (relative intensity): 578 (M^+, 100). Anal. calcd. for $C_{32}H_{18}N_8O_4$: C 66.43, H 3.14, N 19.37; found: C 66.28, H 3.21, N 19.01.

2,9,16,23-Tetrahydroxyphthalocyaninato zinc(II) (11) (1)

Treatment of **8** and **9** as previously described for the preparation of **10** gave **11**. The reaction times were 5 h for both cleavage reactions and gave **11** in 84 and 88% yield, respectively. Alternatively, compound **11** could be prepared from **10** by refluxing **10** with zinc acetate in DMF in 88% yield. Compound **11** was a blue solid, mp >320°C; UV–vis (THF) λ_{max} (log ε): 684 (5.00), 672 (4.90), 614 (4.44), 348 (4.83); IR (KBr, cm^{-1}): 3100–3500 (broad signal, phenolic group), 1600, 1475, 1300, 1240, 1085, 1040, 945, 745; ^{1}H NMR (DMSO-d_6) δ: 10.65–10.63 (m, 4H (phenolic group)), 9.19–9.15 (m, 4H), 8.70–8.68 (m, 4H), 7.67–7.63 (m, 4H); MS (FAB) for $C_{32}H_{16}N_8O_4Zn$, *m/z* (relative intensity): 640 (M^+, 100). Anal. calcd. for $C_{32}H_{16}N_8O_4Zn$: C 59.88, H 2.51, N 17.46, Zn 10.18; found: C 59.70, H 2.80, N 16.99, Zn 10.51.

4-Methoxymethoxyphthalonitrile (15)

Toluenesulfonic acid (TsOH, 150 mg), 4-hydroxyphthalonitrile (**12**) (33) (1.50 g, 10.4 mmol), and dimethoxymethane (**13**) (10 mL) were mixed with 200 mL of dry dichloromethane in a round-bottom flask, equipped with a Soxhlet extractor, in which there was a thimble containing 30 g of 4 Å molecular sieves (29). The suspension was protected under argon and heated under reflux with stirring. After every 12 h, 5 mL of fresh **13** was added. After 24 h, the molecular sieves were replaced with fresh sieves. As the reaction proceeded, the solid gradually dissolved. After 48 h under reflux conditions, the mixture was washed twice with 30 mL of a 0.5 M sodium hydroxide solution, twice with 30 mL of distilled water, and was dried with magnesium sulfate. After filtration and evaporation, 1.81 g of a crude yellowish product was obtained. It was then chromatographed on neutral alumina, eluting with ethyl acetate and hexane (4:6), to give 1.80 g (92%) of pure **15** as white yellowish crystals, mp 80–81°C; UV–vis (dichlorobenzene) λ_{max} (log ε): 304 (3.16), 286 (2.60), 278 (2.54); IR (KBr, cm^{-1}): 3100, 3060, 2980, 2960, 2920, 2220 (CN), 1940, 1780, 1600, 1560, 1495, 1450, 1420, 1320, 1310, 1290, 1240 (C-O-C), 1230, 1170, 1090, 990, 920, 890, 850, 730, 700, 660; ^{1}H NMR ($CDCl_3$) δ: 7.72 (d, J = 8.7 Hz, 1H), 7.45 (d, J = 2.4 Hz, 1H), 7.36 (dd, J = 8.7, 2.5 Hz, 1H), 5.27 (s, 2H), 3.50 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 160.41, 135.20, 121.23, 120.93, 117.44, 115.58, 115.21, 108.34, 94.62, 56.76; MS for $C_{10}H_8N_2O_2$, *m/z* (relative intensity): 188 (M^+, 60), 157 (60), 144 (100), 127 (90), 115 (30), 100 (60). Anal. calcd. for $C_{10}H_8N_2O_2$: C 63.82, H 4.38, N 14.93; found: C 63.82, H 4.29, N 14.88.

4-Ethoxymethoxyphthalonitrile (16)

4-Hydroxyphthalonitrile (**12**) (1.50 g, 10.4 mmol) was mixed with 200 mL of dry dichloromethane in a round-bottom flask equipped with a Soxhlet extractor containing molecular sieves (4 Å, 30 g). Diethoxymethane (**14**) (10 mL) and 150 mg of TsOH were added to the above suspension. The mixture was then heated under reflux with stirring. After every 12 h, 5 mL of fresh diethoxymethane was added. After 24 h, the molecular sieves were replaced by fresh sieves. As the reaction proceeded, the solid gradually dissolved. After 48 h, the mixture was washed twice with 30 mL of sodium hydroxide solution (0.5 M), twice with 30 mL distilled water, and was dried with magnesium sulfate. After filtration and evaporation, 2.01 g of a yellowish solid was obtained. This solid was then further purified on neutral alumina by column chromatography using ethyl acetate and hexane (4:6). After evaporation of the solvent, the residue was recrystallized from methanol and water to give 2.00 g (95% yield) of pure compound **16** as white or yellowish crystals, mp 56–57°C; UV–vis (dichlorobenzene) λ_{max} (log ε): 306 (3.22), 286 (2.71), 282 (2.64); IR (KBr, cm^{-1}): 3120, 3075, 2980, 2935, 2900, 2200 (-CN), 1935, 1590, 1560, 1495, 1480, 1410, 1400, 1320, 1290, 1240 (C-O-C), 1090, 960, 910, 870, 850, 740; ^{1}H NMR ($CDCl_3$) δ: 7.72 (d, J = 8.7 Hz, 1H), 7.45 (d, J = 2.5 Hz, 1H), 7.36 (dd, J = 8.7, 2.5 Hz, 1H), 5.32 (s, 2H), 3.74 (q, J = 7.0 Hz, 2H), 1.22 (t, J = 7.0 Hz, 3H, 3H); ^{13}C NMR (NMR ($CDCl_3$) δ: 160.62, 135.19, 121.23, 120.93, 117.41, 115.63, 108.19, 93.39, 65.39, 16.01; MS for $C_{11}H_{10}N_2O_2$, *m/z* (relative intensity): 202 (M^+, 10), 157 (40), 144 (100), 127 (40), 116 (20), 100 (20). Anal. calcd. for $C_{11}H_{10}N_2O_2$: C 65.35, H 5.27, N 13.80; found: C 65.34, H 4.99, N 13.85.

2,9,16,23-Tetra(methoxymethoxy)phthalocyaninato zinc(II) (17)

A suspension of 500 mg (2.66 mmol) of **15** and 2.5 mL of DBU in 2.5 mL of 1-butanol was stirred and heated under reflux. The phthalonitrile dissolved after 10–20 min. Then, 170 mg (0.93 mmol) of dried zinc acetate was added to the solution. After 24 h under reflux, the dark mixture was poured into 150 mL of methanol and water (1:1) to form a precipitate. The precipitate was collected by centrifugation, and washed with water, methanol, and hexane. The crude product was then purified by column chromatography on neutral alumina, eluting with ethyl acetate and hexane (9:1). Evaporation of the solvent gave 197 mg (36.2%) of a dark blue solid **17**. When the procedure previously described for the preparation of **8** was used to prepare the compound, the yield was 60%; UV–vis (2-methoxyethanol) λ_{max} (log ε): 680 (5.15), 672 (5.16), 610 (4.50), 350 (4.85), 286 (4.46), 240 (4.56); IR (KBr, cm^{-1}): 2950 (br), 1610, 1490, 1400, 1350, 1240 (C-O-C), 1210, 1160, 1050, 1000, 930, 830, 780, 750, 730; ^{1}H NMR (DMSO-d_6) δ: 9.10–7.70 (br, 12H), 5.76 (m, 8H), 3.67 (m, 12H); (pyridine-d_5) δ: 9.54–9.36 (m, br, 8H), 8.71 (m, 4H), 5.79–5.70 (d, 8H), 3.64–3.61 (d, 12H); ^{13}C NMR ($CDCl_3$) δ: 108–158; JMOD ^{13}C NMR (pyridine-d_5) δ: 159.6 (m, 1 × 4C), 153.9–153.2 (m, 2 × 4C), 141.0–140.8 (m, 1 × 4C), 133.1 (m, 1 × 4C), 124.3–123.5 (m, 1 × 4C), 119.6 (m, 1 × 4C), 109.1 (m, 1 × 4C), 95.3 (s, 1 × 4C), 56.3 (s, 1 × 4C). Anal. calcd. for $C_{40}H_{32}N_8O_8Zn$: C 58.72, H 3.94, N 13.70, Zn 7.99; found: C 58.55, H 4.10, N 13.62, Zn 8.12.

2,9,16,23-Tetrahydroxyphthalocyanine (10) from 17

A solution of 82 mg (0.1 mmol) of **17** in 50 mL of hydrochloric acid solution (HCl and 2-methoxyethanol 1:9) was stirred at 80°C overnight and then neutralized with 10% aqueous solution of sodium hydroxide. The solution was then poured into a saturated solution of sodium chloride (150 mL) to precipitate the phthalocyanine. The precipitate was washed twice with water to get rid of sodium chloride and then dissolved in a small portion of DMF and precipitated from toluene to get rid of any incompletely hydrolysed phthalocyanine species. This precipitate was then preabsorbed onto 2 g of classical silica gel and subjected to a classical column chromatography on silica gel, eluting with ethyl acetate and DMF in increasing amounts of DMF. After evaporation of the solvent and precipitation from toluene, 47 mg (31%) of **10** was obtained.

*3-*p-n-*Butylbenzyloxyphthalonitrile (20)*

A procedure previously described for the preparation of **4** (Method II) was used to prepare **20** in 95% yield as white crystals, mp 70–71°C; IR (KBr, cm^{-1}): 3080, 3020, 2950, 2920, 2850, 2250, 2220, 1575, 1470, 1295, 1280, 1180, 1040, 840, 790; ^{1}H NMR ($CDCl_3$) δ: 7.62–7.56 (t, J = 15 Hz, 1H), 7.54–7.16 (m, 7H), 5.24 (s, 2H), 2.64–2.62 (t, J = 15.4 Hz, 2H), 1.62–1.57 (m, 2H), 1.39–1.31 (m, 2H), 0.95–0.90 (t, J = 14.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 161.14, 143.68, 134.44, 131.75, 128.98, 127.34, 125.30, 117.62, 117.22, 115.32, 113.02, 105.53, 71.57, 35.38, 33.51, 22.34, 13.91; MS for $C_{19}H_{18}N_2O$, *m/z* (relative intensity): 291 ($(M + 1)^+$, 18), 247 (20), 147 ($C_4H_9PhCH_{2+}$, 100), 127 (22), 116 (33), 104 (44), 91 (40), 78 (27), 64 (23), 51 (20). Anal. calcd. for $C_9H_{18}N_2O$: C 78.60, H 6.25, N 9.65; found: C 78.92, H 6.12, N 9.83.

*1,8,15,22-Tetra(*p-n-*butylbenzyloxy)phthalocyanine (21)*

Lithium (0.30 g) was suspended in 30 mL of *n*-octanol. The suspension was heated to 170°C under stirring and kept for 4 h. The homogenous solution was cooled to 40°C, at which point was added 0.35 g (1.2 mmol) of **20** in 4 mL of dried THF. The temperature was raised to 60°C and the mixture kept stirring for 2 h. Then, the temperature was raised to 100°C and stirring was continued for 12 h. The temperature was further raised to 120°C, and stirring continued for another 2 h. The mixture was cooled to room temperature and the reaction was

quenched with methanol and water (1:1) to form a blue precipitate. The precipitate was collected by centrifugation, washed successively with water, methanol, and hexane, and dried to give 126.7 mg (40%) of a dark-green solid **21**, mp >320°C; UV–vis (THF) λ_{max} (log ϵ): 724 (4.70), 690 (4.71), 658 (4.02), 627 (2.95), 395 (3.46), 351 (3.96); IR (KBr, cm^{-1}): 3310 (N-H), 3010, 2960, 2920, 2860, 1665, 1530, 1440, 1385, 1240, 1175, 1145, 1110, 1010, 925, 850; ^1H NMR (pyridine-d_5) δ: 9.48–9.45 (d, J = 7.5 Hz, 4H), 8.34–8.32 (d, J = 7.8 Hz, 8H), 8.27–8.22 (t, J = 15 Hz, 4H), 7.91–7.89 (d, J = 8 Hz, 4H), 7.66–7.63 (d, J = 7.7 Hz, 8H), 5.93 (s, 8H), 2.85–2.80 (t, J = 15 Hz, 8H), 1.83–1.73 (m, 8H), 1.51–1.42 (m, 8H), 1.01–0.96 (t, J = 15 Hz, 12H), −4.2 (br, 2H); MS (FAB) for $C_{79}H_{74}N_8O_4$, *m/z* (relative intensity): 1164 ((M + 2)$^+$, 68), 1017 {((M + 2)680 − R)$^+$, 56}, 870 {((M + 2)680 − 2R)$^+$, 23}, 723 {((M + 2)680 − 3R)$^+$, 100}, 578 {((M + 2)680 − 4R)$^+$, 91}. Anal. calcd. for $C_{76}H_{74}N_8O_4$: C 78.46, H 6.41, N 9.63; found: C 78.22, H 6.63, N 9.24.

*1,8,15,22-Tetra(*p-n-*butylbenzyloxy)phthalocyaninato zinc(II) (22)*

Lithium (0.60 g) was suspended in 60 mL of *n*-octanol. The mixture was heated to 170°C and kept stirring for 4 h. The homogeneous solution was cooled to 40°C, at which point was added 0.52 g (1.79 mmol) of **20** in 5 mL of THF. The solution was slowly heated to 100°C and underwent a colour change from colourless to green. To the green solution was added 326 mg (1.79 mmol) of zinc acetate and the solution was kept stirring for 12 h at 100°C. The temperature was raised to 120°C and stirring was continued for another 2 h. The mixture was cooled to room temperature and quenched with methanol and water (1:1) to form a shining, blue precipitate. The precipitate was collected by centrifugation, washed successively with water, methanol, and hexane, and dried. The blue solid was examined under a microscope and exhibited crystalline needles. Further recrystallization from THF gave 0.44 g (80%) of shining, blue, square crystals **22**.

Compound **22** can also be prepared from **21**. A mixture of 80 mg (0.069 mmol) of **15** and 50 mg of zinc acetate in 5 mL of DMF and toluene (1:1) was refluxed for 24 h. To the mixture was added 10 mL of water, and it was then centrifuged to separate a shining, blue solid. The solid was washed with water, methanol, and hexane, and dried to give 76 mg (90%) of a shining, blue solid **22** as needle or square crystals, mp >320; UV–vis (THF) λ_{max} (log ϵ): 696 (5.34), 665 (4.37), 626 (4.46), 369 (4.45); IR (KBr, cm^{-1}): 3010, 2940, 2920, 2840, 1580, 1485, 1335, 1260, 1235, 1130, 1090, 1060, 1040, 1020, 800, 760, 735; ^1H NMR (pyridine-d_5) δ: 9.44–9.41 (d, J = 7.5 Hz, 4H), 8.34–8.31 (d, J = 6.6 Hz, 8H), 8.24–8.19 (t, J = 15.4 Hz, 4H), 7.88–7.86 (d, J = 8.0 Hz, 4H), 7.68–7.63 (d, J = 7.7 Hz, 8H), 5.91 (s, 8H), 2.85–2.80 (t, J = 15.2 Hz, 8H), 1.83–1.73 (p, 8H), 1.51–1.39 (m, 8H), 1.01–0.96 (t, J = 14.6 Hz, 12H); JMOD ^{13}C NMR (pyridine-d_5) δ: 156.85 (s, 1 × 4C), 154.18 (s, 1 × 4C), 154.07 (s, 1 × 4C), 143.01 (s, 1 × 4C), 142.25 (s, 1 × 4C), 135.20 (s, 1 × 4C), 130.91 (s, 1 × 4C), 129.20 (s, 2 × 4C), 128.62 (s, 2 × 4C), 126.41 (s, 1 × 4C), 116.79 (s, 1 × 4C), 113.68 (s, 1 × 4C), 71.40 (s, 14C), 35.84 (s, 4C), 34.20 (s, 4C), 22.72 (s, 4C), 14.25 (s, 4C); MS (FAB) for $C_{76}H_{72}N_8O_4$, *m/z* (relative intensity): 1226 ((M + 2)$^+$, 100), 1079 {((M + 2)fs20 − R)$^+$, 88}, 932 {((M + 2)fs20 − 2R)$^+$, 96}, 785 {((M + 2)fs20 − 3R)$^+$, 84}, 638 {((M + 2)fs20 − 4R)$^+$, 68}. Anal. calcd. for $C_{76}H_{72}N_8O_4Zn$: C 74.41, H 5.92, N 9.13; found: C 74.21, H 5.18, N 9.07.

1,8,15,22-Tetrahydroxyphthalocyanine (23)

To a suspension of 50 mg (0.043 mmol) of **21** in 10 mL of TFA was added 25 mg (0.19 mmol) of TMB. The suspension was refluxed for 50 h. The TFA was evaporated and the residue was washed with hexane. The green residue was dissolved in THF and put onto a gel permeation column, eluting with THF. Evaporation of the solvent gave 6.2 mg of **23** (25% yield) as a green solid; UV–vis (THF): λ_{max} (log ϵ): 743 (4.69), 7.10 (4.69), 680 (4.00), 648 (2.98), 350 (3.40); IR (KBr, cm^{-1}): 3100–1500 (broad signal, phenolic group), 1620, 1482, 1310, 1284, 1220, 1200, 1095, 1000, 930, 820, 745, 710 cm; ^1H NMR (DMSO-d_6) δ: 10.50 (s, 4H), 8.51–8.45 (d, J = 7.5 Hz, 4H), 8.07–8.05 (t, J = 15 Hz, 4H), 7.68–7.65 (d, J = 7.5 Hz, 4H), −3.5 (br, 2H); MS (FAB) for $C_{32}H_{18}N_8O_4$, *m/s* (relative intensity): 578 (M$^+$, 100).

1,8,15,22-Tetrahydroxyphthalocyaninato zinc(II) (24)

To 109 mg (0.086 mmol) of **22** in 5 mL of TFA was added 46 mg (0.35 mmol) of TMB. The mixture was refluxed for 15 h. The TFA was evaporated and the residue was washed a few times with hexane. The blue solid was dissolved in THF and the solution was put onto a gel permeation column, eluting with THF. Evaporation of the solvent gave 46.8 mg (85%) of **24** as a blue solid; UV–vis (THF) λ_{max} (log ϵ): 719 (4.85), 686 (4.12), 646 (4.13), 344 (4.06); IR (KBr, cm^{-1}): 3100–3500 (broad signal, phenolic group), 1650, 1520, 1430, 1360, 1275, 1215, 1060, 925, 840; ^1H NMR (DMSO-d_6) δ: 10.56 (s, 4H), 8.58–8.56 (d, J = 7.5 Hz, 4H), 8.28–8.22 (t, J = 15 Hz, 4H), 7.83–7.81 (d, J = 7.7 Hz, 4H); MS (FAB) for $C_{31}H_{16}N_8O_4Zn$, *m/z* (relative intensity): 640 (M$^+$, 100). Anal. calcd. for $C_{32}H_{16}N_8O_4Zn$: C 59.88, H 2.51, N 17.46; found: C 59.74, H 2.33, N 16.89.

Acknowledgements

This research was supported by grants from the Natural Sciences and Engineering Research Council of Canada (NSERC).

1. I. Rosenthal, E. Ben-Hur, S. Greenberg, A. Concepcion-Lam, D.M. Drew, and C.C. Leznoff. Photochem. Photobiol. **46**, 959 (1987).
2. B. Paquette and J.E. van Lier. *In* Photodynamic therapy: basic principles and clinical aspects. *Edited by* B.W. Henderson and T.J. Dougherty. Marcel Dekker, New York. 1992. p. 145.
3. I. Rosenthal. Photochem. Photobiol. **53**, 859 (1991).
4. J.E. van Lier. *In* Photodynamic therapy of neoplastic disease. Vol. 1. *Edited by* D. Kessel. CRC Press, Boca Raton, Fla. 1990. p. 279.
5. I. Rosenthal and E. Ben-Hur. *In* Photodynamics: properties and applications. Vol. 1. *Edited by* C.C. Leznoff and A.B.P. Lever. VCH, New York. 1989. p. 393.
6. E. Ben-Hur, I. Rosenthal, and C.C. Leznoff. J. Photochem. Photobiol. B: **2**: 243 (1988).
7. C.C. Leznoff, S. Vigh, P.I. Svirskaya, S. Greenberg, D.M. Grew, E. Ben-Hur, and I. Rosenthal. Photochem. Photobiol. **49**, 79 (1989).
8. R.W. Boyle, C.C. Leznoff, and J.E. van Lier. Br. J. Cancer, **67**, 1177 (1993).
9. M.C. Venuti, B.E. Loe, G.H. Jones, and J.M. Young. J. Med. Chem. **31**, 2132 (1988); H. Schmidhammer and A. Brossi. J. Org. Chem. **48**, 1469 (1983); J.D. White and J.C. Amedio, Jr. J. Org. Chem. **54**, 736 (1989).
10. L. Lapatsanis. Tetrahedron Lett. 3943 (1978); V.G. Miranovski. Angew. Chem. Int. Ed. Engl. **15**, 281 (1976).
11. S.K. Chaudhary and O. Hernandez. Tetrahedron Lett. 95 (1979); S. Hanessian and A. P.A. Staub. Tetrahedron Lett. 95 (1973).
12. C.B. Reese. *In* Protective groups in organic chemistry. *Edited by* J.F.W. McOmie Plenum Press, New York. 1973. p. 104; T.W. Greene. *In* Protective groups in organic synthesis. Wiley, New York. 1981. p. 187.
13. R.C. Larock. Comprehensive organic transformations. VCH, New York. 1989.
14. L.F. Fieser and M. Fieser. Reagents for organic synthesis. Vol. 1. Wiley, New York. 1967. p. 132; J.F.W. McOmie. Adv. Org. Chem. **3**, 191 (1963); R.L. Edwards and I. Mir. J. Chem. Soc. [C], 411 (1967).
15. C.C. Leznoff. *In* Phthalocyanines — properties and applications. Vol. 1. *Edited by* C.C. Leznoff and A.B.P. Lever. VCH, New York. 1989.
16. S. Greenberg, A.B.P. Lever, and C.C. Leznoff. Can. J. Chem. **66**, 1059 (1988).
17. I.G. Oksengendler, N.V. Kondratenko, E.A. Luk'yanets, and L.M. Yagupol'skii, Zh. Org. Khim. **13**, 2234 (1977).
18. M. Hanack, G. Rene, J. Strahle, and S. Schmid. J. Org. Chem. **66**, 3501 (1991).
19. M. Hanack, G. Schmid, and M. Sommerauer. Angew. Chem. Int. Ed. Engl. **32**, 1422 (1993).
20. D.M. Drew and C.C. Leznoff. Synlett. In press. 1994.
21. W.O. Siegl. J. Heterocycl. Chem. **18**, 1613 (1981).

22. S.W. Oliver and T.D.J. Smith. Heterocycles, **22**, 2407 (1984).
23. H. Tomoda, S. Saito, S. Ogawa, and S. Shiraishi. Chem. Lett. 1277 (1980).
24. R. Davis and J.M. Muchowski. Synthesis, 987 (1982); T. Katsuki, A.W.M. Lee, P. Ma, V.S. Martin, S. Masamune, K.B. Sharpless, D. Tuddenham, and F.J. Walker. J. Org. Chem. **47**, 1378 (1982).
25. J.R. Medich, K.B. Kunnen, and C.R. Johnson. Tetrahedron, 4131 (1987); S. Hanessian, T.J. Liak, and B. Vanasse. Synthesis, 396 (1981); V.S. Rao and A.S. Perlin. Carbohydr. Res. **83**, 175 (1980); A.M. Felix, E.P. Heimer, T.J. Lambros, C. Tzougraki, and J. Meienhofer. J. Org. Chem. **43**, 4194 (1978).
26. H. Sakuri, A. Shirahata, K. Sasaki, and A. Hosomi. Synthesis, 740 (1979); M.E. Jung and M.A. Lyster. J. Org. Chem. **42**, 3761 (1977); G.A. Olah, S.C. Narang, B.G. Gupta, and R. Malhotra. Angew. Chem. Int. Ed. Engl. **18**, 612 (1979); J. Org. Chem. **44**, 1247 (1979).
27. J. Mayrargue, M. Essamkaou, and H. Moskowitz. Tetrahedron Lett. 6867 (1989); Y. Kiso, K. Ukawa, K. Nakamura, K. Ito, and T. Akita. Chem. Pharm. Bull. **28**, 673 (1980); C.N.. Kornblum and A. Scott. J. Am. Chem. Soc. **96**, 590 (1974).
28. H. Yoshino, Y. Tsuchiya, I. Saito, and M. Tsujii. Chem. Pharm. Bull. 3438 (1987).
29. J.P. Yardley. U.S. Patent 3,987,105 (1976); Chem. Abstr. **86**, 5148q (1977).
30. S.M. Marcuccio, P.I. Svirskaya, S. Greenberg, A.B.P. Lever, C.C. Leznoff, and K.B. Tomer. Can. J. Chem. **63**, 3057 (1985).
31. D. Wöhrle, J. Gitzel, I. Okuro, and S. Aono. J. Chem. Soc. Perkin Trans. 2, 1171 (1985).
32. P.J. Duggan and P.F. Gordon. Eur. Pat. Appl. Ep 155780 (1985); Chem. Abstr. **105**, 72642 (1987).
33. V.A. Ustinov, V.V. Plakhtinskii, G.S. Mironov, and N.S. Ryabukhina. Zh. Org. Kh. **15**, 1775 (1979).