Phthalocyanines: The Need for Selective Synthetic Approaches

Gema de la Torre,[a] Christian G. Claessens,[a] and Tomás Torres*[a]

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Recent years have witnessed increasing interest in the synthesis of low-symmetry single phthalocyanines (Pcs) since they may show, among other applications and advantages, interesting second-order nonlinear optical (NLO) properties. This potential of unsymmetrically substituted and regioisomerically pure phthalocyanines has motivated researchers in this field to develop selective methods for synthesizing macrocycles of this type. In this microreview, we focus on the approaches reported by other research groups as well as ourselves that allow the predominant or exclusive formation of the required compounds. The selective preparation of differently substituted or intrinsically unsymmetrical Pc-related systems and Pc homologues is also discussed.

Introduction

Phthalocyanines (Pcs)[1] are 18 π-electron aromatic macrocycles comprising four isoindole units linked together through their 1,3-positions by aza bridges. The particular two-dimensional π-electron delocalization over these macrocycles gives rise to a great number of unique physical properties. Thus, Pcs are chemically and thermally stable compounds that exhibit exceptional optical and electrical behaviour. For these reasons, they find wide application in the area of materials science. Other remarkable features that increase their usefulness are their versatility and tailorability; several chemical modifications can be made at the Pc ring, thereby allowing a fine-tuning of their physical properties. Phthalocyanines are capable of incorporating more than 70 different metallic and nonmetallic cations in their ring cavity. It is also possible to attach a wide variety of substituents at the periphery of the macrocycle, which can alter the electronic structure of the system, and, when these groups are bulky or long-chain

[a] Departamento de Química Orgánica (C−I), Universidad Autónoma de Madrid,
Cantoblanco, 28049 Madrid, Spain
Fax: (internat.) + 34-1/397-3966
E-mail: tomas.torres@uam.es

Gema de la Torre was born in Madrid, Spain, in 1969. She studied Chemistry at the Universidad Autónoma de Madrid (UAM). She obtained her Ph. D. in 1998, working on the chemistry of phthalocyanines at the UAM under the supervision of Professor T. Torres. Since 1997 she has been Teaching Assistant at the Department of Organic Chemistry (UAM), where she is currently working in the synthesis and physical properties of new phthalocyanine derivatives.

Christian G. Claessens was born in Valenciennes, France, in 1969. He performed his undergraduate education at the Ecole Normale Supérieure de Lyon, France. He received his Ph.D. in Organic Chemistry from the University of Birmingham, England, in 1997, under the supervision of Professor J. Fraser Stoddart. Following a one-year period as a postdoctoral fellow in Professor André Collet's group in the Ecole Normale Supérieure de Lyon, he joined Professor Tomás Torres' group at the Autónoma University of Madrid as a Marie Curie postdoctoral fellow. His current research interests include the synthesis and applications of subphthalocyanines.

Born in 1951, Prof. Tomás Torres is Vice Director of the Department of Organic Chemistry at the Autonoma University of Madrid (UAM). After his Ph.D. (1978), he spent two years at the Max-Planck Institute for Biochemistry (in Martinsried near Munich, Germany). Then he joined (1981) a private company, Abello S.A. − Merck, Sharp and Dohme, in Madrid. In 1985 he moved to the UAM. He is interested in organic synthesis, supramolecular chemistry and molecular materials based on phthalocyanine derivatives. He is the author of ca. 150 research papers and patents.

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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hydrophobic moieties, can serve to increase the solubilities of Pcs in common organic solvents. Another approach employed for modulating the properties of Pcs is the rational modification of their skeletons. To this end, several structural changes have been made to the ring, leading to various Pc analogues, the most common approaches being extension of the π-system, variation of the number of isoindole units, and formal replacement of some of the isoindole units by other (hetero)cyclic moieties. An additional remarkable feature of Pcs and analogues is their ability to form a wide range of condensed phases with controlled molecular architectures, such as discotic liquid crystals and thin films, which may exhibit responses at a supramolecular level. Notably, phthalocyanine-based thin films have found application in a wide range of technological areas, e.g. in gas sensors,[2] electrochromic devices,[3] photovoltaic materials,[4] etc. Phthalocyanines are also attracting interest in other areas, such as photodynamic therapy[5] and nonlinear optics.[6,7]

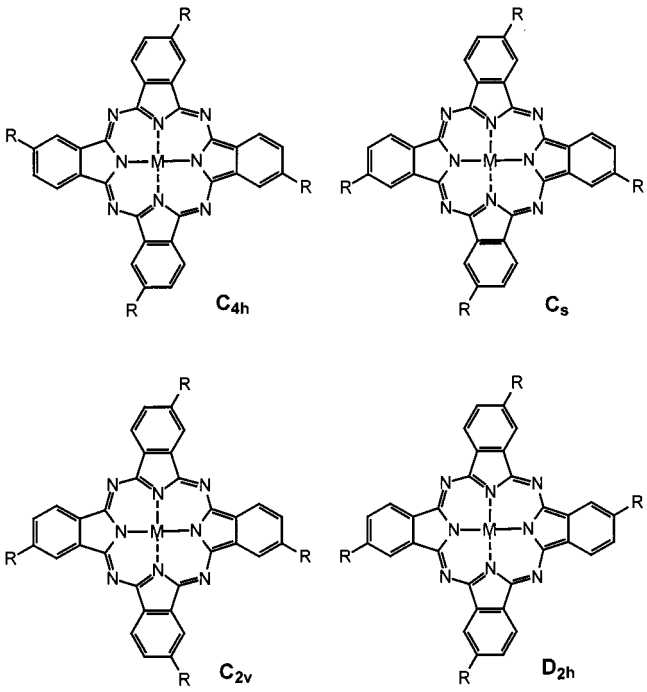
The syntheses[1] of the most widely described unsubstituted or symmetrically substituted Pcs have been accomplished in moderate yields by cyclotetramerization reactions of phthalyl derivatives, usually a phthalonitrile or a 1,3-diiminoisoindoline. However, very recently, a great deal of attention has been paid to the preparation of low-symmetry Pc and Pc-related systems,[8] obtained either by introducing different substituents on the macrocyclic ring or by formal substitution of some isoindolic units, since these may show new physical properties and improved organization capabilities. For example, such noncentrosymmetric systems can exhibit second-order nonlinear optical properties, whereas unsubstituted or symmetrically substituted Pcs usually only give rise to third-order responses. When the preparation of an unsymmetrically substituted phthalocyanine is undertaken by mixed condensation of two different phthalonitriles, a mixture of compounds is obtained and the desired Pc has to be isolated by means of chromatographic techniques. This nonselective method usually leads to poor yields of the desired unsymmetrical Pc and hence many attempts have been made to solve this problem.

On the other hand, noncentrosymmetric Pcs are also obtained when an unsymmetrically substituted precursor without a mirror plane perpendicular to the aromatic ring is used, e.g. a monosubstituted phthalonitrile. In such cases, the reaction leads to a mixture of isomers. Among other applications and advantages, pure isomers may show interesting second-order NLO properties that cannot be investigated in the mixture of all four possible isomers.

In the present article, we focus on the approaches developed by other research groups as well as ourselves that allow the predominant or exclusive formation of the desired regioisomerically pure or unsymmetrically substituted compounds. The methods developed for the selective preparation of differently substituted or intrinsically unsymmetrical Pc-related systems are discussed. We also deal with the selective approaches developed for obtaining or isolating one single isomer of tetrasubstituted Pcs.

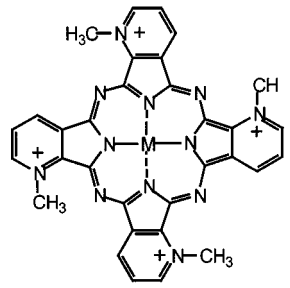
Advances in the Preparation of Single Constitutional Isomers

The geometrical combination of four identical diiminoisoindoline subunits lacking C_{2v} symmetry in a phthalocyanine framework leads to four constitutional isomers with C_s, D_{2h}, C_{2v}, and C_{4h} symmetries (Scheme 1).



Scheme 1

A statistical mixture of these four isomers would contain 12.5% of the D_{2h} isomer, 12.5% of the C_{4h} isomer, 25% of the C_{2v} isomer, and 50% of the C_s isomer. This fact, first recognized[9] by Linstead in 1936 in the course of studies on the synthesis of 1,2-naphthalocyanines, led organic chemists first to separate and characterize each isomer and then to design selective synthetic pathways. Even if the presence of different isomers was acknowledged, it was often impossible to characterize or separate them as a consequence of their low solubilities and/or the propensities of Pcs to form aggregates. The introduction of new solubilizing and nonaggregating substituents coupled with the refinement of ^{1}H NMR spectroscopy allowed first the detection of the isomers and then their separation by HPLC on specially designed phases. The first direct observation of the existence of phthalocyanine constitutional isomers was achieved by ^{1}H NMR spectroscopy in 1985 by Wöhrle and coworkers.[10] Mixtures of isomers of a quaternized tetra-2,3-pyridinoporphyrazine (Scheme 2) could be isolated, but unfortunately it was impossible to unambiguously identify each isomer in the mixture or to separate them further.



Scheme 2

Two methods have proved useful for the selective synthesis of only one of the four possible constitutional isomers of Pcs: appropriate modifications of the *statistical approach* and what we might call the *directed approach*. The former is based on variations of the substitution pattern of the starting phthalonitrile or on tuning of the reaction conditions so as to improve the selectivity. The latter involves specially designed bis(phthalonitrile) derivatives that can yield only one Pc constitutional isomer.

Statistical Approach

When a 4-substituted phthalyl derivative is employed as starting material, a mixture of all four isomers is obtained irrespective of the reaction conditions. In 1993, Hanack and co-workers succeeded in separating the four constitutional isomers of [tetrakis(2-ethylhexyloxy)phthalocyaninato]nickel(II) for the first time by HPLC[11] and, in 1996, they undertook a thorough study of the isomer ratio of a family of 2(3),9(10),16(17),23(24)-substituted Pcs with newly developed HPLC phases based on (*p*-butyldinitrophenyl)quinoline-modified silica gel.[12] The four constitutional isomers of these tetrasubstituted Pcs, bearing bulky alkyloxy and thio substituents, were obtained in a statistical ratio, irrespective of the reaction conditions.

On the other hand, the introduction of a substituent at the 3-position of the starting material led to results that were strongly dependent on the reaction conditions used. Many research groups have claimed good or total selectivities in the formation of the C_{4h} isomer when starting from 3-substituted phthalonitrile derivatives in the presence of lithium alcoholates. It has been demonstrated that this type of reaction is strongly dependent on (i) the temperature, and (ii) the alcoholate employed. For example, Leznoff and co-workers, in attempting to synthesize 3-alkyloxy-substituted Pcs at low temperature (i.e. at room temperature or up to 50 °C instead of the standard 140 °C), observed the selective formation of the C_{4h} isomer when working with Li/octanol as a base.[13] A steric effect was ruled out since use of the less hindered 1,2-dicyano-3-methoxybenzene also led to 100% of the C_{4h} isomer under the same conditions. Kasuga and co-workers[14] studied the isomer distribution as a function of the reaction temperature for various 3-alkyloxy-substituted phthalonitrile molecules using Li/pentanol as a base. They observed highly favoured formation of the C_{4h} isomer (up to 86% with respect to all the isomers), but also noticed that the selectivity towards the C_{4h} isomer formation increases with decreasing reaction temperature. These studies also showed that 3-substituted phthalonitrile derivatives do not react at all below 80 °C, highlighting a significant difference between the use of lithium pentanolate and octanolate in the selectivity of Pc formation.

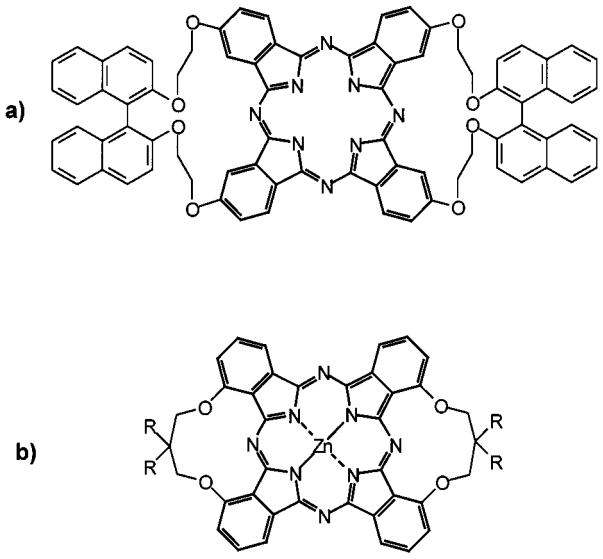
In order to clarify the aforementioned results, Hanack and co-workers[15] carried out a systematic study of the selectivity of phthalocyanine formation by varying the reaction conditions, the central metal atoms, and the positions of the substituents on the diiminoisoindole units. It now seems clear from this survey that two mechanisms of Pc formation are involved. The first operates under basic conditions (Li/alcohol), involves 3-alkyloxy-1-imidoindolines as intermediates, and is mainly driven by a difference of charge distribution between the two cyano groups of a single unit. In the case of a 3-substituted starting phthalonitrile, the charge distribution is sufficiently different to induce the formation of a greater proportion of the C_{4h} isomer (up to 87% of all isomers). On the other hand, both cyano groups of a 4-substituted phthalonitrile possess the same charge distribution and therefore under these conditions the reaction leads to a near statistical mixture of the four isomers.

The second mechanism is operative in the presence of a metal template such as Zn^{II}, Ni^{II}, or Cu^{II}. In a polar solvent, four phthalonitrile units coordinate about the central metal core either before or during the cyclotetramerization. This mechanism does not introduce selectivity when 3- or 4-substituted dicyano derivatives are employed; isomer distributions close to the statistical one are obtained, with the exception of the low D_{2h} isomer proportion (2−3% instead of the expected 12.5%) when a 3-substituted phthalonitrile derivative is employed. This may be a consequence of the two unfavorable steric interactions that would be involved during the formation of this isomer. These studies also revealed that the selectivity depends very little on the metal template. Surprisingly, when a chiral substituent was introduced in the 3-position of a dicyano derivative, the resulting phthalocyanine isomer mixture was found to contain a high proportion of the C_{4h} isomer with respect to the statistical distribution (up to 29% instead of 12.5%) or with respect to the same reaction with the corresponding racemate (29% instead of 10% in one case).[15]

The Directed Approach

Another approach towards the selective synthesis of a single constitutional isomer, termed the "directed approach", involves the rational design of phthalonitrile precursors, cyclotrimerization reactions of which may only lead to one isomer. In this way, it has been shown to be possible to obtain exclusively the D_{2h} isomer simply by symmetrically linking two phthalonitrile units with appropriate spacers. Kobayashi and co-workers obtained a chiral D_{2h} isomer by linking two phthalonitrile units at their 4-positions with optically active 2,2′-dihydroxy-1,1′-binaphthyl[16] (Scheme 3a). Leznoff and co-workers generated solely the

D_{2h} isomer when they employed a dimer composed of two phthalonitrile units linked through their 3-positions with a 2,2-disubstituted propan-1,3-diol spacer[17] (Scheme 3b).



Scheme 3

Selective Synthesis of Unsymmetrically Substituted Phthalocyanines

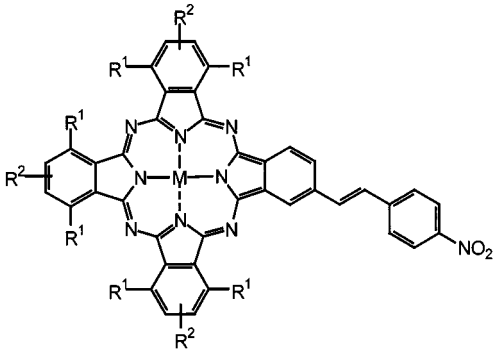
For some years, researchers working in the area of Pc chemistry have endeavoured to develop selective methods for the synthesis of unsymmetrically substituted phthalocyanines, basically those containing two different isoindole subunits (i.e. A and B). Depending on the type of product one wishes to obtain (A_3B or A_2B_2), specific approaches can be applied for the preparation of the desired compound.

Synthesis of A_3B Phthalocyanines

Statistical Condensation

Considering that symmetrically substituted Pcs are usually synthesized by cyclotetramerization reactions of phthalonitriles or 1,3-diiminoisoindolines, the most simple approach to the preparation of phthalocyanines bearing different substituents is the mixed condensation of two differently substituted precursors. In principle, this is a nonselective method affording a mixture of six compounds, thus necessitating the use of chromatographic techniques in order to isolate the desired macrocycles. Furthermore, it has been widely reported that such statistical mixtures are difficult to separate due to the tendency of Pc molecules towards aggregation. Although selectivity has not been achieved using this method, some approaches have been developed with a view to increasing the yield of the required compounds.

The statistical condensation is generally utilized for the preparation of Pcs comprising of one different and three identical isoindole subunits (A_3B),[18] which for years have been targets of choice for second-order NLO applications.[19] In particular, we have endeavoured to prepare phthalocyanines in which the A moiety of the macrocycle bears donor groups and the B moiety bears electron-withdrawing groups, or vice versa (Scheme 4),[19c−19f] as such a substitution pattern confers an unsymmetrical charge distribution on the molecule, a necessary feature for achieving second-order NLO effects. However, other strategies must be used for the synthesis of A_2B_2 derivatives, as we discuss below, since they are composed of a mixture of two isomers, the "*adjacent*" (AABB) and "*opposite*" (ABAB) compounds. There have been very few examples of the separation of macrocycles of this type from statistical mixtures by column chromatography.[20]



a $R^1 = H$, $R^2 = C(CH_3)_3$
b $R^1 = C_8H_{17}$, $R^2 = H$
c $R^1 = OC_8H_{17}$, $R^2 = H$

Scheme 4

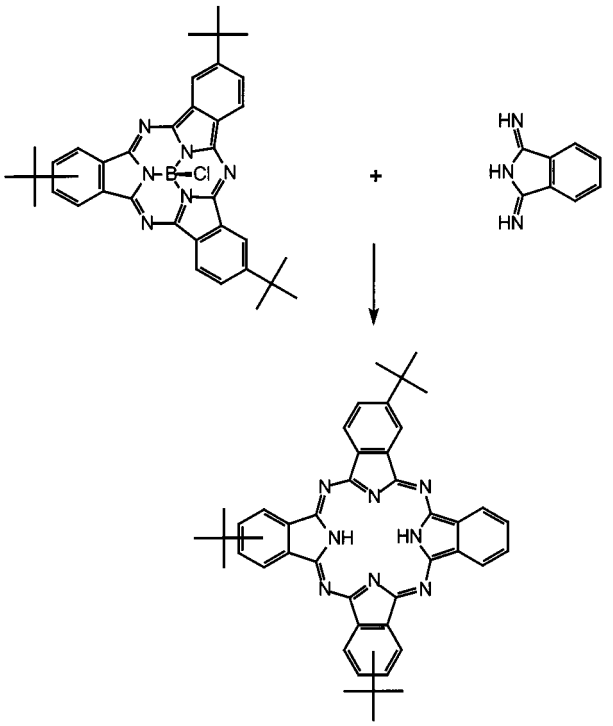
In order to favour the formation of the A_3B derivative, appropriate stoichiometric ratios of the two reactants A and B have to be employed. Statistical considerations predict that reaction of two different phthalyl derivatives of the same reactivity in a 3:1 ratio will afford a mixture of products in the following percentages: A_4 (33%), A_3B (44%), other cross-condensation products (23%). Commonly, 3:1 molar ratios are employed, which afford the desired compounds in yields ranging from 10 to 20%.[18] It is always preferable to use phthalonitriles with different solubility characteristics as this may permit separation of the unsymmetrical Pcs by virtue of the different solubilities of the compounds present in the resulting statistical mixture. Thus, the attachment of *tert*-butyl groups or hydrocarbon chains at the 3,6-positions of one of the starting compounds (usually the one used in excess) (Scheme 4) facilitates the isolation of the A_3B product, as these substituents render the Pc soluble and disfavour aggregation of the macrocycles. McKeown has also demonstrated that excellent chromatographic separation can be achieved with complex mixtures of Pcs having varying degrees of alkyl and oligo(oxyethylene) substitution due to the dissimilar polarities of these two types of side chains.[21] The presence of dendritic substituents has also been shown to facilitate the separation of the required A_3B phthalocyanine.[22]

Cook and co-workers usually employ these 3,6-disubstituted phthalonitriles (A) in a 9:1 ratio with respect to the

other phthalonitrile (B). Although this ratio leads to an increase in the amount of A_4 and decreases the amount of the desired A_3B, no other cross-condensation products are formed and the required compound (A_3B) can easily be separated from this simple mixture.[23] This 9:1 stoichiometry is also useful when B is much more reactive than A,[19c][19d] as we have pointed out previously, because it reduces the yields of products with more than one B subunit.

A procedure that reduces the number of possible Pcs and also suppresses the aggregation between them involves the use of a phthalonitrile (A) bearing bulky and rigid groups, e.g. phenyl, in the 3,6-positions, in conjunction with another phthalonitrile lacking bulky substituents (B).[20b,20c,24]

It has been reported by Kobayashi[24] that two units of A cannot be adjacent and coplanar due to steric hindrance, and hence only the less congested Pcs are formed in the statistical reaction, i.e. BBBB, BBBA, and BABA. Hanack and co-workers have detected the additional formation of AABB and AAAB derivatives in low yields, the BBBA product being the major component of the reaction mixture when a 1:1 ratio is used.

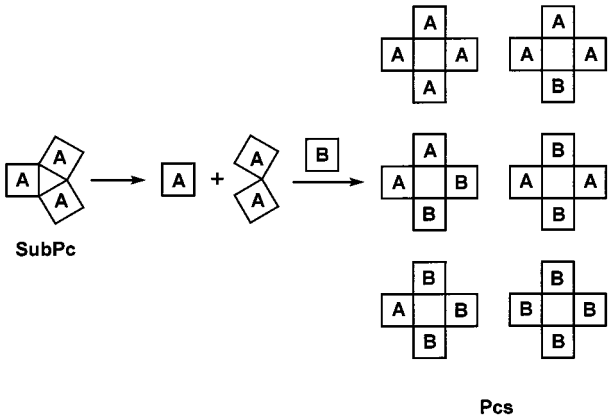


Scheme 5

The Subphthalocyanine Approach

An original method for the selective synthesis of unsymmetrically substituted phthalocyanines of type A_3B, developed in the late 1980s by Kobayashi and others,[25−27] involves ring expansion of a subphthalocyanine (SubPc) by treating it with a succinimide or diiminoisoindoline derivative (Scheme 5). Thus, the geometrically constrained subphthalocyanine core is readily cleaved in the presence of a diiminoisoindoline unit, which is then incorporated into its framework so as to form a phthalocyanine derivative of type A_3B. This reaction has proved to be very selective and efficient in some cases, and it has also allowed the synthesis of previously unattainable phthalocyanines.[28,29]

From the results obtained by us and others,[30−34] it is now clear that the outcome of this synthetic method depends very much on the reaction conditions and on the characteristics of the starting materials. A typical ring expansion is accomplished by the addition of a 6−9 molar excess of the diiminoisoindoline derivative to a solution of the subphthalocyanine in DMSO/1-chloronaphthalene or dichlorobenzene (1:4 to 4:1) or (dimethylamino)ethanol, and leaving the reaction mixture at 80−100 °C for 5−12 h. The desired unsymmetrically substituted Pcs are obtained in yields ranging from 3−90%. In 1995, we suggested[28] that the reaction proceeds through partial or total fragmentation of the subphthalocyanine ring followed by statistical ring closure of the fragments, giving rise to a mixture of all possible phthalocyanines containing all the combinations of diiminoisoindoline units present in the starting materials (Scheme 6). It was also demonstrated[30] by Wöhrle and co-workers that the addition of a metal template to the reaction mixture increased the yields of both the desired A_3B unsymmetrically substituted phthalocyanine and of the other products. It has also been shown that SubPcs can react with less reactive phthalonitrile derivatives in the presence of a strong base such as DBU, giving rise to good yields of the A_3B phthalocyanine.[30] By comparing the yields of the same A_3B unsymmetrically substituted phthalocyanine achieved by ring expansion or by statistical condensation, it appeared[31] that the first method is more efficient even though, as in the present case, the yields for both methods are fairly low (< 15%). Kinetic studies by UV/Vis spectrophotometry of the ring expansion, monitoring the appearance of the Pc Q-band at around 650 nm and the disappearance of the SubPc Q-band at 570 nm, showed a first-order rate with respect to the subphthalocyanine starting material.[32,33]



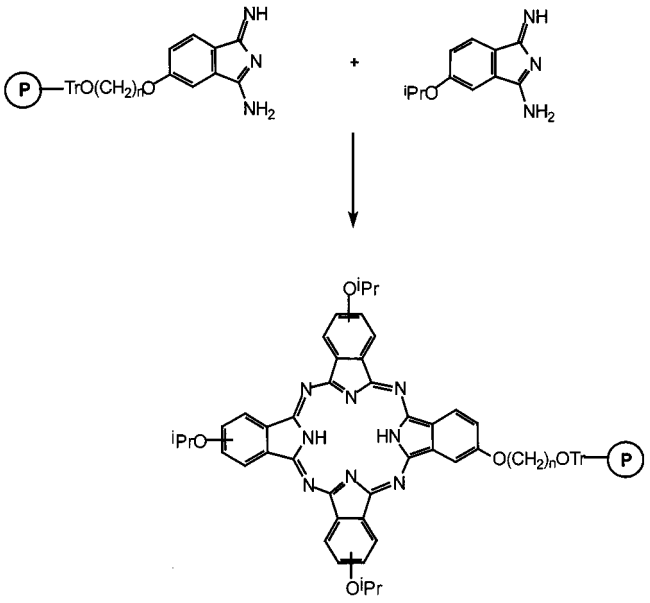
Scheme 6

The best yields and selectivities were obtained in the case of ring expansions between less reactive SubPcs bearing no substituents or electron-withdrawing ones and diiminoisoindoline derivatives bearing electron-donor groups. The ring expansion of subphthalocyanines has in some cases

proved to be an excellent route to unsymmetrically substituted phthalocyanines of the A_3B-type. More widespread use has been limited only by its unpredictability, although this will probably be eliminated once the mechanism of the ring expansion is better understood.

Polymeric Support Method

Another approach for the selective preparation of A_3B phthalocyanines, mainly developed by Leznoff, is the solid-phase synthesis.[35] This method involves the attachment of an appropriately substituted phthalonitrile (B) to a polymeric support. This insoluble polymer-bound precursor can then be treated with another differently substituted unbound phthalonitrile (A), giving rise to a polymer-bound A_3B phthalocyanine. This can be easily separated from the A_4 macrocycle since the symmetrical phthalocyanine can be washed away. The desired A_3B phthalocyanine is subsequently liberated from the polymer support. Leznoff et al. have mainly used polymers with pendant alcohol groups (Scheme 7) and have treated these with 4-nitrophthalonitriles.[35a][35b] Further cleavage at the pendant chain furnishes the unsymmetrical phthalocyanine in yields of around 20−25%. Modified silica gels have been successfully utilized by other groups as supports for solid-phase reactions of this kind.[35c]



Scheme 7

This approach is restricted to the use of phthalonitriles bearing functional groups that can be bound to the polymer and subsequently cleaved from it. However, considering the current expansion of solid-phase technology and the wide variety of commercially available solid phases, this is a very promising route for the selective synthesis of unsymmetrically substituted A_3B Pcs.

Synthesis of A_2B_2 Phthalocyanines

As mentioned above, A_2B_2 derivatives can rarely be isolated from statistical mixtures; they are composed of a mixture of two isomers, ABAB and AABB, which show similar solubility characteristics and are frequently eluted in the same fraction. However, during the last decade, specific methods have emerged for the exclusive preparation of one of the two macrocycles.

Crosswise-Substituted Phthalocyanines (ABAB)

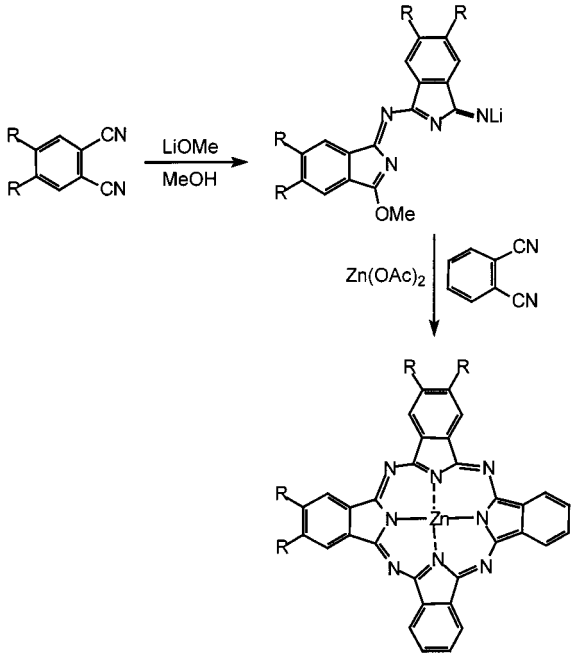
In 1990, Young et al. followed a patented method[36] for the selective synthesis of these D_{2h} symmetry derivatives,[37] which are attractive building blocks for the preparation of Pc-based ladder polymers.[38] This procedure involved the synthesis of phthalocyanines under mild conditions from equivalent amounts of two different phthalyl derivatives, namely 1,3-diiminoisoindoline and 1,3,3-trichloroisoindolenine, in the presence of a base and a reducing agent. The yields obtained by this reductive coupling process were significantly high (ca. 50%) and the authors claimed that only the ABAB derivative was formed under these conditions. Other groups have applied such methodology in order to obtain these D_{2h} phthalocyanines, but the yields reported have been lower than those achieved by Young (15−25%).[38,39] In particular, Hanack and co-workers have reported the additional formation of the AAAB derivative as a by-product.[38] In all cases, this route affords the desired compound with high selectivity.

Another reported example of a cross-condensation reaction is that involving 1,3-diiminoisoindoline and 1*H*-isoindole-1,3(2*H*)-dithione in a 1:1 molar ratio.[40] In this case, the unsymmetrical ABAB phthalocyanine was found to be contaminated with traces of all the other possible phthalocyanines.

"Adjacent" Phthalocyanines (AABB)

Recently, Leznoff and co-workers have described an approach for the preparation of AABB compounds. This method involves the use of a "half-Pc" intermediate, which can be isolated and subsequently treated with another phthalonitrile under very mild conditions (Scheme 8).[41] The preparation of half intermediates had been reported previously,[42] but it was proposed that only phthalonitriles bearing strongly electron-withdrawing groups could give rise to such stable intermediates. In Leznoff's work, treatment of 4,5-bis(3,3-dimethyl-1-butynyl)phthalonitrile with lithium alkoxide in refluxing methanol gave the corresponding intermediate, which was then treated with phthalonitrile in a second step (Scheme 8) to furnish the AABB phthalocyanine in 20% yield, along with some amounts of other possible Pcs. This strategy needs to be refined in order to obtain only the desired AABB Pc and to make it applicable as a general method for the preparation of "adjacent" substituted phthalocyanines bearing any types of functional groups.

The synthesis of AABB derivatives has also been undertaken by Kobayashi,[43] using bis(phthalonitriles) linked by appropriately constrained bridging groups, such as 2,2′-dihydroxy-1,1′-binaphthyl. Such precursors can react with other differently substituted phthalonitriles to furnish the adjacent-type Pcs in 20−25% yield.



Scheme 8

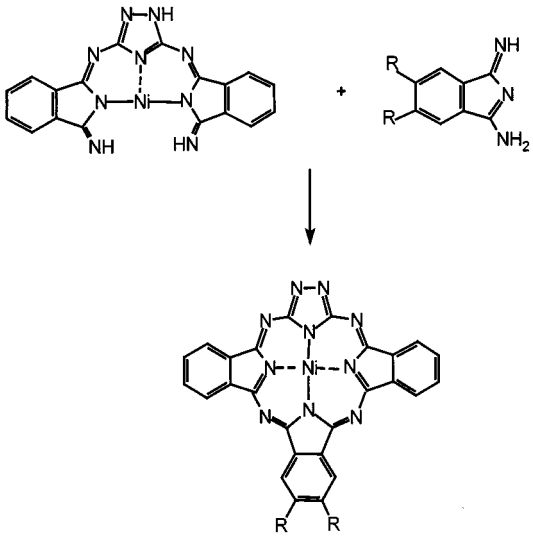
Some Trends in the Selective Synthesis of Low-Symmetry Phthalocyanine Analogues

The chemical flexibility of porphyrin-like metallomacrocycles related to phthalocyanines, such as porphyrazines, hemiporphyrazines, Pc homologues, etc., provides an excellent opportunity for the selective preparation of single constitutional isomers and unsymmetrical analogues of these compounds. Herein, we focus in particular on the preparation of triazole-containing macrocycles and on a family of lower Pc homologues, namely the subphthalocyanines (SubPcs), fields in which our research group has been actively involved in the last few years.

Triazole-Containing Macrocycles

The noncentrosymmetry that has been pursued in phthalocyanines with the A_3B substitution pattern can easily be achieved in some phthalocyanine analogues. Modification of the macrocyclic structure affords low-symmetry analogues with total selectivity. Thus, the formal substitution of only one isoindole subunit A in a phthalocyanine by another conjugated (hetero)cyclic moiety furnishes noncentrosymmetric phthalocyanine analogues with an A_3B pattern, in which B is the nonisoindole (hetero)cyclic moiety (e.g. benzene, pyridine, pyrrole, thiadiazole, triazole...). The introduction of this new heterocyclic unit may preserve the porphyrazine character, giving rise to the widely investigated tribenzoporphyrazines,[44,45] or disrupt it. The latter modification leads to the so-called *three-quarter phthalocyanines*.

One of the most striking changes to the Pc core, as carried out by our research group, is the incorporation of a triazole moiety into the structure, giving rise to the three-quarter derivatives termed *triazolephthalocyanines*.[46] These intrinsically unsymmetrical macrocycles are isoelectronic with phthalocyanines and retain some of the exceptional physical and optical properties of the latter. Their synthesis can be accomplished by a template-assisted mixed condensation of 3,5-diamino-1,2,4-triazole (guanazole) and 1,3-diiminoisoindoline in the appropriate ratio.[47] Furthermore, our group has reported a stepwise strategy (Scheme 9) for the selective preparation of unsymmetrically substituted triazolephthalocyanines,[48] involving the preformation of a three-unit metal complex by reaction of guanazole and 1,3-diiminoisoindoline, which is subsequently treated with a further 1,3-diiminoisoindoline unit. This flexible method, typically giving yields in the range 35−60%, has allowed us to introduce differently substituted isoindole moieties into the triazole core, thereby permitting a fine-tuning of the physical properties the resulting compounds.

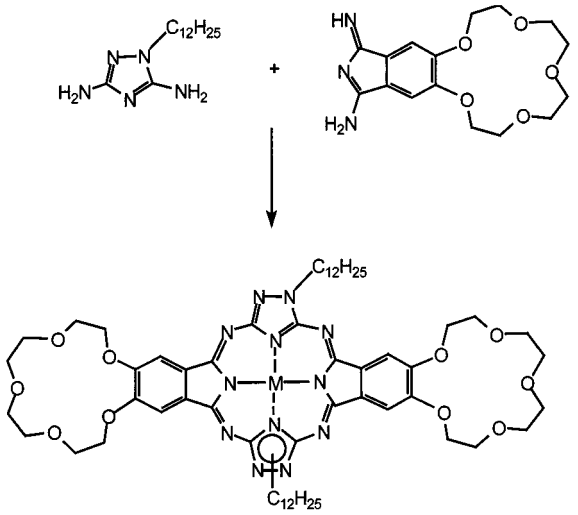


Scheme 9

On the other hand, A_2B_2 Pc analogues are also appealing target systems in the area of macrocyclic chemistry. Hemiporphyrazines[49] are two-dimensional π-conjugated macrocycles related to phthalocyanines composed of two isoindole units and two (hetero)aromatic moieties bridged through aza functions. These ABAB-type macrocycles are usually prepared by mixed condensation of a 1,3-diiminoisoindoline derivative and a diamino-substituted (hetero)aromatic component in a 1:1 ratio. Although 1,3-diiminosoindoline could cyclotetramerize to phthalocyanine, no traces of this compound are detected in the crude mixtures and only the desired cross-condensation takes place. This chemoselectivity may be emulated in the formation of ABAB-type Pcs through the selection of two suitably substituted phthalonitrile derivatives that would exclusively undergo cross-condensation. For example as a consequence of the different electronic characters of each phthalonitrile moiety.

In this area, our group has mainly worked with the family of *triazolehemiporphyrazines* (Scheme 10),[49] which are synthesized by treating a 1,3-diiminoisoindoline with an appropriate 3,5-diamino-1,2,4-triazole.[50] In view of the extreme insolubility of the unsubstituted parent macrocycle, we have

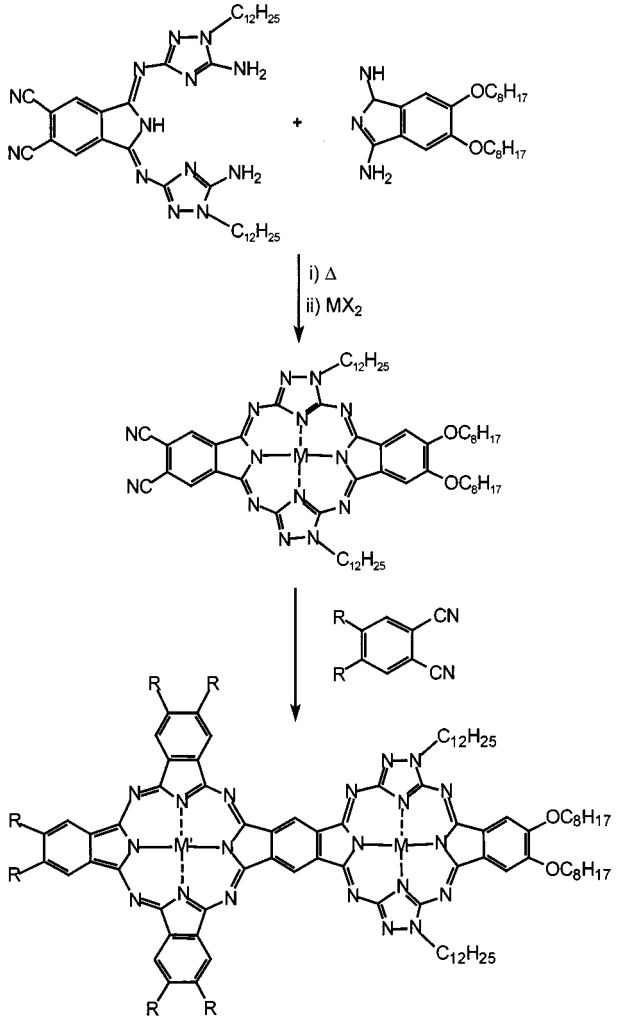
made efforts to introduce lipophilic substituents in either the triazole or isoindole moieties,[49,51] and it has been shown that *N*-triazole substitution is an essential feature for high solubility. Thus, the statistical reaction of an *N*-substituted guanazole and a suitably functionalized 1,3-diiminoisoindoline always furnishes a mixture of two regioisomers (Scheme 10), owing to the relative positions of the substituents attached to the triazole moiety. The number of isomers may be increased if unsymmetrically substituted 1,3-diiminoisoindolines are reacted.



Scheme 10

Following our work in this area, we have developed a stepwise general approach for the selective preparation of noncentrosymmetric triazolehemiporphyrazines as single regioisomers (Scheme 11).[52] This method involves the selective preparation of a three-unit compound by reaction of 5,6-dicyano-1,3-diiminoisoindoline with 1-dodecylguanazole. This intermediate can be isolated as a single "*syn*" isomer in 45% yield and subsequently treated with a differently substituted 1,3-diiminoisoindoline to afford regioisomerically pure unsymmetrically substituted triazolehemiporphyrazines in yields ranging from 60−80%.

Moreover, functionalization of these macrocycles with *o*-cyano groups allows the preparation of heterobinuclear phthalocyaninato-triazolehemiporphyrazinate complexes (Scheme 11)[53] through the statistical condensation of the metallo(triazolehemiporphyrazine) with an appropriate phthalonitrile. The large dimensions of the dicyanotriazolehemiporphyrazine starting material rule out the possibility of forming self-condensation products, so that only the fused phthalocyanine-triazolehemiporphyrazine and the symmetrically substituted phthalocyanine arising from the dicyano derivative are isolated from the crude mixture. These compounds can be viewed as noncentrosymmetric phthalocyanines having extended π-conjugation.

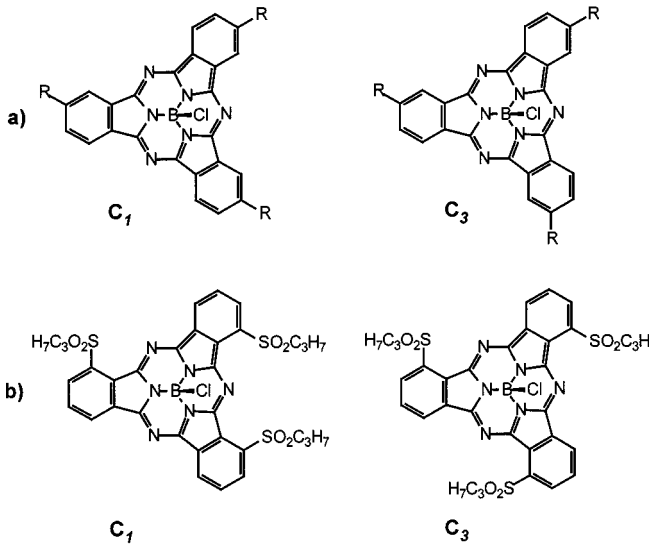


Scheme 11

Subphthalocyanines

As mentioned above, subphthalocyanines[54] are important starting materials for the preparation of unsymmetrically substituted Pcs. Moreover, the singular cone-shaped structures of these 14π-electron aromatic compounds allows the classification of some of their representatives as intrinsically unsymmetrical Pc analogues. Subphthalocyanines prepared from phthalonitriles lacking C_{2v} symmetry potentially consist of mixtures of two constitutional isomers with C_1 and C_3 symmetries (Scheme 12). Compared to their higher phthalocyanine homologues, studies of subphthalocyanines are still at an early stage, even though they have already displayed very interesting physical properties.[55−57]

Few studies have hitherto been carried out aimed at rationalizing or checking the selectivity of SubPc formation. In 1995, Hanack and co-workers[58] separated the constitutional isomers of tri-*tert*-butyl-substituted SubPc and confirmed that they were formed in a 3:1 ratio (C_1/C_3, Scheme 12a), as would be expected for a statistical outcome of the reaction. Recently, a nonstatistical ratio has been observed in the formation of α-substituted SubPcs[59] (Scheme 12b). Thus, reaction of 3-propylsulfonyl-1,2-dicyanobenzene in the presence of BCl_3 in 1-chloronaphthalene affords the C_1 and C_3 constitutional isomers in a 9:1 ratio, in marked contrast to the statistical value. These results were rationalized on the basis of a mechanism involving a dimeric intermediate, the formation and further reaction of



Scheme 12

which show a marked dependence on the steric hindrance brought by the substituents on the starting phthalonitriles.

Very few examples of unsymmetrically substituted SubPcs have been described so far.[60,61] On the basis of the published results, it is still very early to draw reasonuble conclusions concerning the selectivity of the process. This rapidly emerging field should soon yield interesting results and insight into the mechanism of formation of SubPcs.

Conclusions

Efforts are being made in the field of phthalocyanines towards the development of chemo-, regio-, and even stereoselective synthetic methods for the preparation of suitably functionalized systems. Chiral analogues of many phthalocyanine derivatives[15][62] can be expected to be synthetic targets in the near future. On the other hand, the greater chemical flexibility of related porphyrazines facilitates the selective synthesis of low-symmetry single compounds. The last area is beginning to take shape as a promising field of research.

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