LEABHARLANN CHOLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH | TRINITY COLLEGE LIBRARY DUBLIN
Ollscoil Átha Cliath | The University of Dublin

Terms and Conditions of Use of Digitised Theses from Trinity College Library Dublin

Copyright statement

All material supplied by Trinity College Library is protected by copyright (under the Copyright and Related Rights Act, 2000 as amended) and other relevant Intellectual Property Rights. By accessing and using a Digitised Thesis from Trinity College Library you acknowledge that all Intellectual Property Rights in any Works supplied are the sole and exclusive property of the copyright and/or other IPR holder. Specific copyright holders may not be explicitly identified. Use of materials from other sources within a thesis should not be construed as a claim over them.

A non-exclusive, non-transferable licence is hereby granted to those using or reproducing, in whole or in part, the material for valid purposes, providing the copyright owners are acknowledged using the normal conventions. Where specific permission to use material is required, this is identified and such permission must be sought from the copyright holder or agency cited.

Liability statement

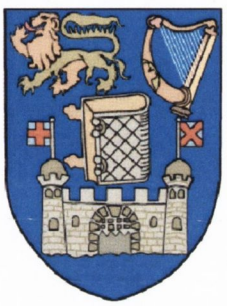
By using a Digitised Thesis, I accept that Trinity College Dublin bears no legal responsibility for the accuracy, legality or comprehensiveness of materials contained within the thesis, and that Trinity College Dublin accepts no liability for indirect, consequential, or incidental, damages or losses arising from use of the thesis for whatever reason. Information located in a thesis may be subject to specific use constraints, details of which may not be explicitly described. It is the responsibility of potential and actual users to be aware of such constraints and to abide by them. By making use of material from a digitised thesis, you accept these copyright and disclaimer provisions. Where it is brought to the attention of Trinity College Library that there may be a breach of copyright or other restraint, it is the policy to withdraw or take down access to a thesis while the issue is being resolved.

Access Agreement

By using a Digitised Thesis from Trinity College Library you are bound by the following Terms & Conditions. Please read them carefully.

I have read and I understand the following statement: All material supplied via a Digitised Thesis from Trinity College Library is protected by copyright and other intellectual property rights, and duplication or sale of all or part of any of a thesis is not permitted, except that material may be duplicated by you for your research use or for educational purposes in electronic or print form providing the copyright owners are acknowledged using the normal conventions. You must obtain permission for any other use. Electronic or print copies may not be offered, whether for sale or otherwise to anyone. This copy has been supplied on the understanding that it is copyright material and that no quotation from the thesis may be published without proper acknowledgement.

Synthesis of Biomedical Relevant Porphyrins



by

Yasser Mohamed Shaker Abdelrahman Atta

B.Sc. (Chemistry), Mansoura University, Egypt & M.Sc. (Organic Chemistry),
Cairo University, Egypt

A thesis submitted to the University of Dublin for the degree of

Doctor of Philosophy

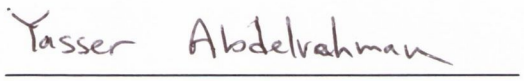
2006 Trinity College Dublin

TRINITY COLLEGE
P 2 1 NOV 2007
LIBRARY DUBLIN
THESIS
8201

Declaration

This thesis has not been submitted as an exercise for a degree at this or any other university. Except where otherwise indicated, the work described herein has been carried out by the author alone.

The author agrees that the library may lend or copy this thesis upon request.



Yasser M. Shaker Abdelrahman

Summary

The research carried out in the present study focuses mainly on the synthesis of functionalized, unsymmetrically substituted porphyrins for potential applications in photodynamic therapy.

Chapter 1 introduces the different classes of porphyrins and describes the most significant general methodologies employed for the synthesis of various classes of meso-substituted porphyrins.

The symmetric porphyrin starting materials (A_2-porphyrins) are easily prepared by simple condensation reactions of dipyrromethane and suitable aldehydes. These porphyrins are then functionalized by a nucleophilic aromatic substitution reaction (S_NAr) with a wide variety of aliphatic, aromatic and functionalized organolithium reagents.

Chapter 2 is concerned with an efficient synthesis of novel A_2BC-porphyrins bearing highly reactive centers in substituents at the meso positions using corresponding functionalized organolithium reagents *via* two-step reactions.

Chapter 3 describes the one-pot synthesis of A_2BC-porphyrins with different functional groups in the meso-positions using organolithium reagents and different alkyl/aryl iodides. The reaction mechanism for the A_2BC-porphyrin formation is also postulated.

Chapter 4 is concerned with one-pot synthesis of ABCD-porphyrins with different functional groups in the meso-positions using functionalized organolithium reagents and different alkyl/aryl iodides. In addition, the synthesis of ABCD-porphyrins *via* two-step reactions is also reported. New ABC-porphyrins were also formed during the ABCD-porphyrins synthesis which are reported, too.

Chapter 5 focuses on the synthesis of novel chlorins, phlorins and porphodimethenes *via* the reaction of functionalized A_4-porphyrins with different organolithium reagents. The impact of the electronic effect of the functional groups in the A_4-porphyrins and the steric effect of the organolithium reagents have been examined.

Comparative studies of the ^1H NMR spetroscopic pattern of the β-pyrrole protons of various A_2-, A_2B-, A_2BC-, ABC- and ABCD-porphyrins are performed. The β-pyrrole protons show clear dependance on the type, number, and arrangement of various substituents in the meso positions of the synthesized porphyrin molecules.

Starting from the medical applied science oriented approach, this study shows how the present tools of synthetic porphyrin chemistry can be combined together to obtain a wide variety of

unsymmetrically substituted amphiphilic porphyrins as potential photosensitizers in photodynamic cancer therapy.

The methodology developed expands present synthetic approaches and opens a practical way to synthesize more highly functionalized substituted porphyrins with a mixed hydrophilic/hydrophobic substitution pattern for the optimization of PDT drugs.

Publications

1. Arno Wiehe, Yasser M. Shaker, Johan C. Brandt, Stefan Mebs, Mathias O. Senge., Lead structures for applications in photodynamic therapy. Part 1: Synthesis and variation of *m*-THPC (Temoporfin) related amphiphilic A_2BC-type porphyrins, *Tetrahedron,* **2005**, *61*, 5535–5564.

2. Yasser M. Shaker, Mathias O. Senge., One-pot synthesis of A_2BC-type free base porphyrins, *Heterocycles,* **2005**, *65*, 2441–2450.

Conference Abstract

One-pot synthesis of free base ABCD- and A_2BC-type unsymmetrically substituted tetrapyrroles: Yasser M. Shaker, Mathias O. Senge *International Conference of porphyrins and Phthalocyanines (ICPP-4) in Rome, Italy*, July 2-7, **2006**.

For my parents

Acknowledgements

Firstly, I wish to express sincere thanks to my supervisor Prof. Mathias O. Senge for his invaluable help and guidance over the years coupled with an expert knowledge during the course of this work from the beginning of my research work with him in Potsdam University, Germany and finally in Trinity College Dublin, Ireland. It has been my honor to work in his research group.

Thanks also to Prof. Corish for the use of the facilities at Trinity College, to Dr. John O`Brien and Dr. Manuel Rüether for the countless NMR samples and their enthusiasm, to Dr. Martin Feeney for the accurate masses, to Fred and Ed in the stores for their endless supply of chemicals and all the technical and administrative staff, especially Brendan within the School of Chemistry, Trinity College Dublin, Ireland.

Many thanks to World Laboratorty (WL), Switzerland, for awarding me a research fellowship as one of the better ways of helping Developing Countries via promoting the participation of their scientific elite in collaboration with Developed Countries and East-West/North-South scientific cooperation.

Many thanks to my coworkers in the School of Chemistry, Trinity College Dublin, Ireland: Dr. Nataliya Sergeeva, Dr. Eleni Notaras, Dr. Oliver Locos, Julia Richter, Katja Dahms, Monica Pintea, Marijana Fazekas, Sabine Horn, Mohd Bakri Bakar, Eimear Finnigan, Remon Remmers, Vanessa Lopez-Pablo and Yulia Sergeeva.

A special word of thanks to Institute of Chemistry, Potsdam University, Germany, for all the facilities provided and also to my coworkers there: Dr. Claudia Ryppa, Viraj Mehta, Sascha Prentzel, Mandy Donath and Ines Bastian.

A humongous thanks to all my German, Irish and Arabic friends in Berlin, Potsdam and Golm (Germany), and in Dublin (Ireland) and the rest of the world for our brilliant time and when trying to let me forget about chemistry!

Thanks to my family for their kind support even if we do not get to see each other very often.

Finally, my deepest gratitude goes to my parents for the love you have extended, always trusting me and supporting me throughout all my years in Germany and Ireland. How do you do it? I would have not got through without you. Thanks also for trying many times to stop me for working in the weekends and I am sorry for not doing that sometimes! Now it is time for us to relax (a little!). I am forever indebted. Thank you!

Abbreviations

Ar	Aromatic
$AsPh_3$	Triphenylarsine
n-BuLi	*n*-Butyllithium
sec-BuLi	*sec*-Butyllithium
t-BuLi	*tert*-Butyllithium
b.p.	Boiling point
CH_2Cl_2	Dichloromethane
$CDCl_3$	Deuterated chloroform
d	Doublet
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DMF	Dimethylformamide
EA	Ethylacetate
Hz	Hertz
Hp	Hematoporphyrin
HpD	Hematoporphyrin derivative
HRMS	High Resolution Mass Spectrometry
$HBF_4.O(Et)_2$	Tetrafluoroboric acid in diethyl ether
IUPAC	International Union of Pure and Applied Chemistry
J	Coupling constant measured by Hertz
$LiAlH_4$	Lithium aluminum hydride
m.p.	Melting point
m	Multiplet
NMR	Nuclear Magnetic Resonance
ppm	Parts per million
PDT	Photodynamic Therapy
Ph	Phenyl
$Pd(PPh_3)_4$	Tetrakis(triphenylphosphine)palladium(0)
P°	Ground state of porphyrin photosensitizer
$^1P^*$	Singlet excited state porphyrin photosensitizer
$^3P^*$	Triplet excited state porphyrin photosensitizer

R.T.	Room Temperature
R_f	Retention factor
RLi	Organolithium reagent
RI	Alkyl iodide reagent
s	Singlet
m-THPP	5,10,15,20-Tetra(3-hydroxyphenyl)porphyrin
m-THPC	5,10,15,20-Tetra(3-hydroxyphenyl)chlorin (Temoporfin)
p-$TPPS_4$	5,10,15,20-Tetra(4-sulfonato-phenyl)porphyrin
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
H_2(TPP)	5,10,15,20-Tetraphenylporphyrin
UV	Ultraviolet
δ	Chemical shift
λ	Wavelength

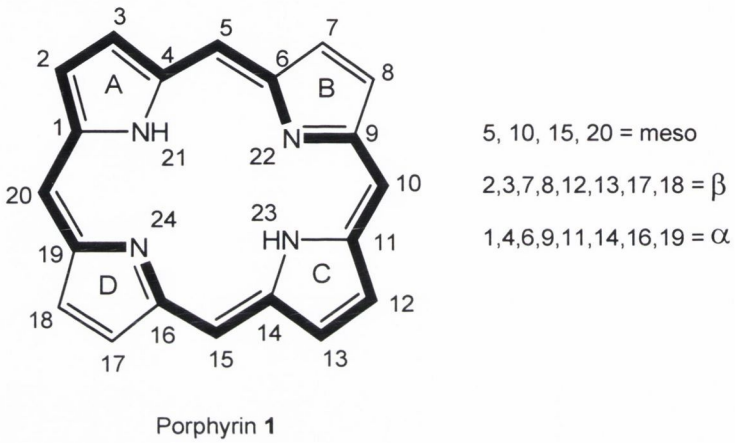
Table of contents

Chapter 1

Introduction

1.1 Overview of the structure and nomenclature of porphyrin

The porphyrin macrocycle **1** is an aromatic system containing 22 π electrons, but only 18 of them are involved in the cyclic delocalization pathway in accord with Hückel`s [4n + 2] rule for aromaticity (n = 4).[1,2] It has been shown by X-ray crystallography to be planar and the basic structure of porphyrin consists of four pyrrole units (A, B, C and D) linked by four methine bridges (Figure 1.1). Its structure is described as a "tetrapyrrole" macrocycle to emphasize its four-rings-within-a-ring pattern.



Porphyrin **1**

Figure 1.1. Numbering scheme used for porphyrins.

According to the IUPAC system of the nomenclature of tetrapyrroles, the 24 macrocycle atoms are numbered from 1 to 24.[3] Four different positions of the atoms are present in the porphyrin system: (1) the four pyrrole nitrogen atoms; (2) the methine bridge carbons which are named meso carbons; (3) the α-pyrrole carbons and the β-pyrrole carbons (Figure 1.1).[4a]

1.2 Different classes of porphyrins

Crystalline and concentrated solutions of porphyrins **1** are typically dark red to purple due to the highly conjugated double-bond structure of the tetrapyrrole ring. It is clear from Figure 1.1 that porphyrins have two peripheral double bonds which are not incorporated into the delocalization pathway. Thus, one or two of them can undergo addition reactions to form chlorins **2** or bacteriochlorins **3** without substantial loss of the macrocyclic aromaticity. Isobacteriochlorins **4** is an isomeric form bacteriochlorins **3**. In **3**, two pyrrole rings with reduced exterior double bonds are opposite each other, but isobacteriochlorins **4** consists of

two pyrrole rings with reduced double bonds that are adjacent to one another. Porphyrinogens **5** are reduced porphyrins that contain six additional hydrogen atoms and electrons. As seen in Figure 1.2, porphyrinogens lack the highly conjugated double-bond structure found in porphyrins, are colorless and do not fluoresce in solution. Porphyrinogens are unstable and rapidly oxidized to their corresponding porphyrins.[4b] Saturation of one meso position in a porphyrin causes an interruption in the macrocyclic conjugation to form phlorins **6** which bear one meso-sp^3 hybridized carbon. Porphodimethenes **7** are known to be an intermediate between porphyrinogen **5** and porphyrin **1** and have two meso-sp^3 hybridized carbons which therefore interrupts the conjugation pathway.[4c]

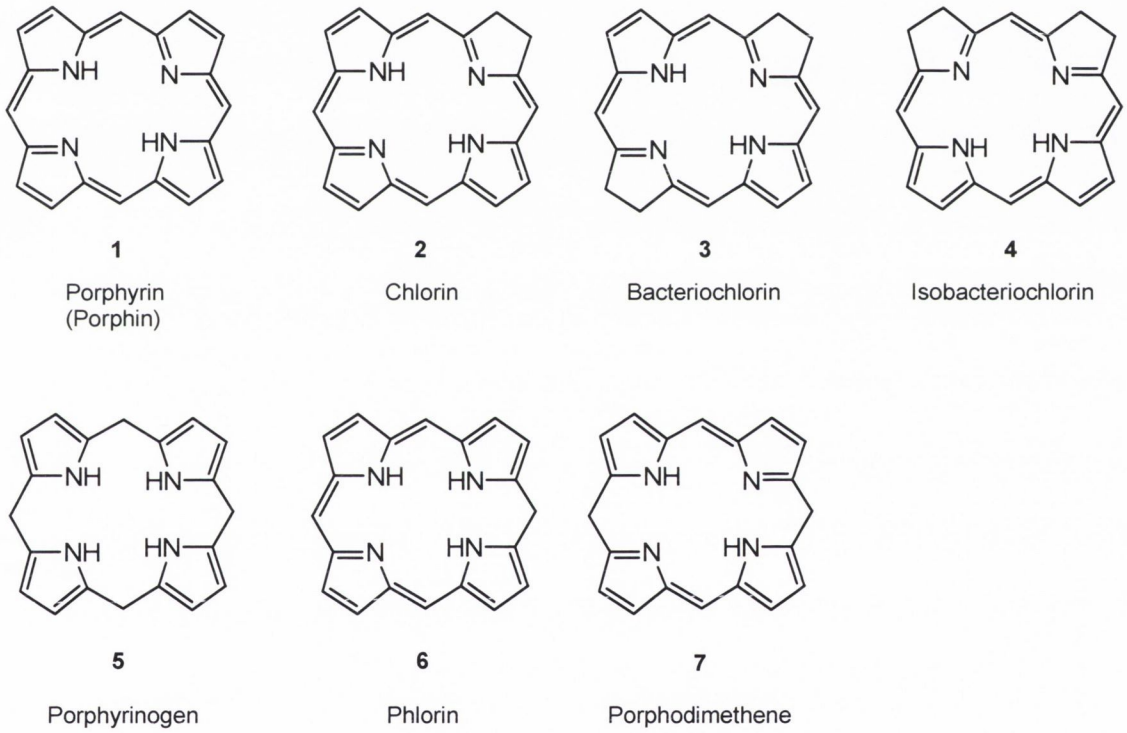


Figure 1.2. Different tetrapyrrole classes.

1.3 meso-Substituted porphyrins

1.3.1 Reactivity of the meso positions

Simple generalizations on the reactivity of porphyrins, based on valence bond considerations, were proposed by Woodward in 1962;[5] these predicted greater electrophilic character for the meso positions relative to the β-pyrrolic positions on the porphyrin macrocycle. This

prediction was rationalized based on the idea that the two pyrrolenine units in porphyrins tend to achieve an individual aromatic sextet of electrons; this withdraws electron density from the neighboring meso carbons, rendering them more electrophilic. More general reactivity patterns were derived from theoretical *ab initio* self-consistent field-molecular orbital (SCF-MO) calculations;[6] the result of which predicts that most reactions occurring with porphyrins (electrophilic aromatic substitutions, electrophilic and nucleophilic additions, radical reactions) take place preferentially at the meso positions. Although electronically more reactive, the meso positions are sterically less accessible, especially when one or two of the abutting β-positions are substituted. The β-pyrrolic positions are sterically favored and, as a result, undergo substitution and addition reactions.

1.3.2 Classes of meso-substituted porphyrins

Figure 1.3 shows that porphyrins may have different degrees of meso-substitution. These are:

(1) Monosubstitution: A-type

(2) Disubstitution: four types (two symmetric A_2 and two unsymmetric AB).

(3) Trisubstitution: four types (A_3, two types of A_2B and ABC).

(4) Tetrasubstitution: Seven types (A_4, A_3B, two types of A_2B_2, two types of A_2BC and ABCD).

Indeed, meso-substituted porphyrins bearing specific patterns of functional groups are valuable components in the synthesis of porphyrin-based biomimetic system and materials chemistry. The substituents at the meso positions may include alkyl, aryl, heterocyclic or organometallic groups, as well as other porphyrins. The main emphasis in the next part will be on the various methods for synthesizing meso-substituted porphyrins.

1.3.3 Synthesis of meso-substituted porphyrins

Synthetic control over the molecular entities attached at the porphyrin periphery enables porphyrins to be designed and tailored for specific applications. The popularity of meso-substituted porphyrins stems from their ease of synthesis and amenability toward synthetic elaboration. One-flask synthetic methods can be used to prepare a meso-substituted porphyrin from an aldehyde and pyrrole. A wide availability and ease of manipulation of aldehydes enable diverse porphyrins to be constructed without extensive multistep syntheses of precursors. The variety of methods for synthesizing meso-tetra-substituted porphyrins *via* one-

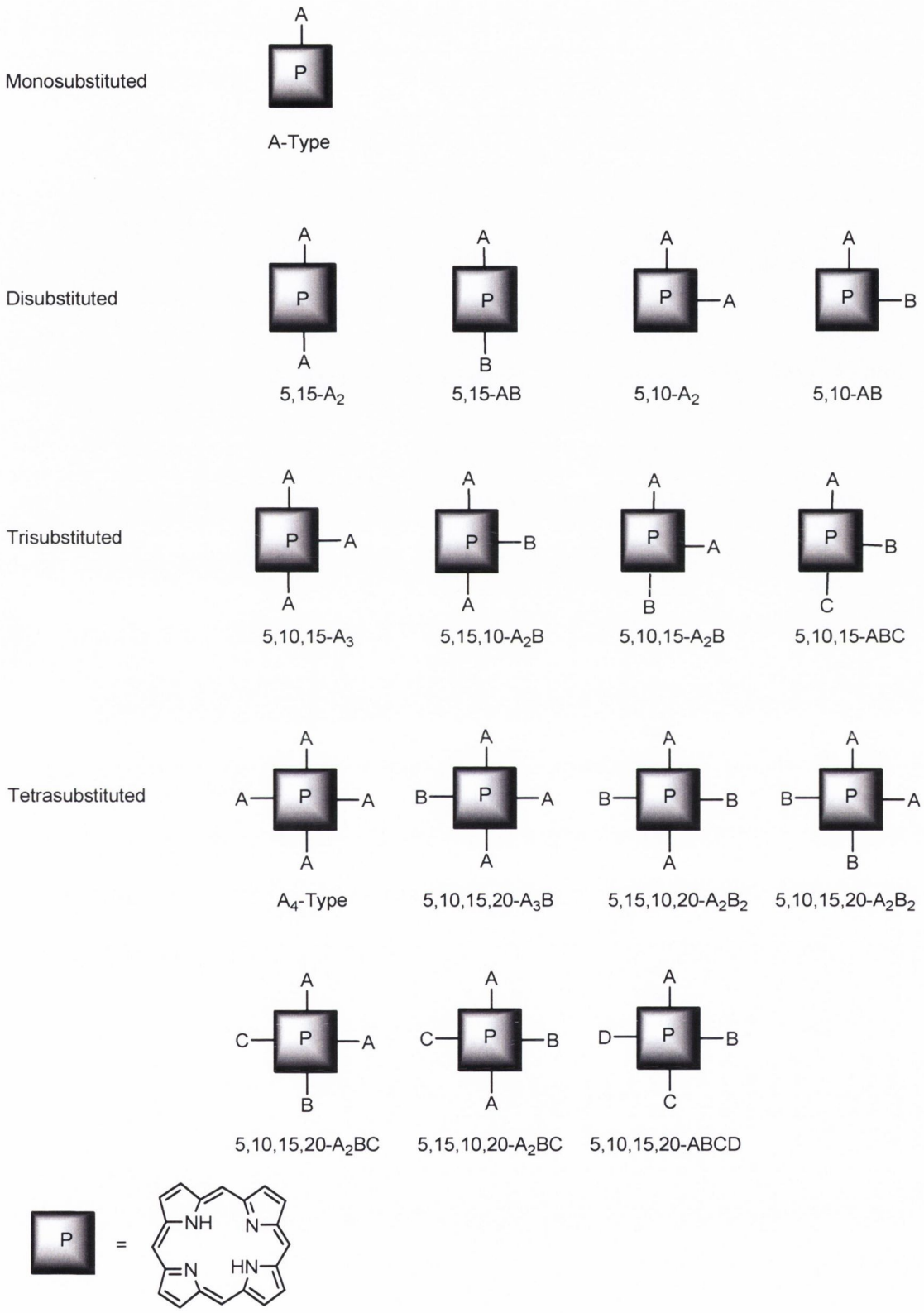
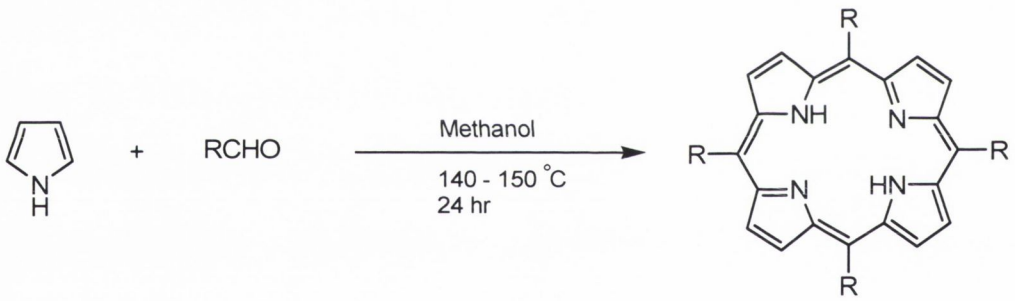


Figure 1.3. Definition of the different classes of the *meso*-substituted porphyrin.

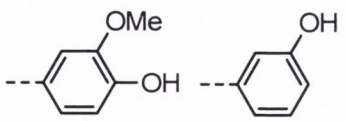
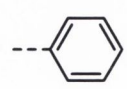
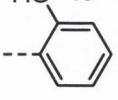
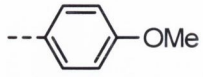
flask methods and the stepwise synthesis of porphyrins having designated patterns of up to four different meso-substituents will now be discussed. The medicinal applications of the substituted porphyrins in photodynamic therapy (PDT) will be described subsequently.

A. Rothemund Method

Rothemund first investigated the synthesis of 5,10,15,20-tetramethylporphyrin by condensing acetaldehyde and pyrrole in methanol at various temperatures in 1935.[7] The completely unsubstituted porphyrin, porphine, was synthesized subsequently. Heating a solution of ~ 0.44 M pyrrole and ~ 0.58 M formaldehyde in methanol under a nitrogen atmosphere in a sealed vessel at 90 — 95 °C for 30 h gave porphine in 0.9 % yield.[8] In this manner, crystallized porphyrins were obtained from propionaldehyde, *n*-butyraldehyde, benzaldehyde and *α*-furaldehyde. Similar reactions at 140 — 150 °C for 24 h were applied to the synthesis of porphyrins **8-16** (Scheme 1.1).[9]



8-16

R	
Aliphatic	Aromatic
CH_3 : **8**	 **12**
$CH_3CH_2CH_2$: **9**	**15**
$CH_3CH_2CH_2CH_2$: **10**	 **13**
$(CH_3)_2CHCH_2$: **11**	 **16**
	 **14**

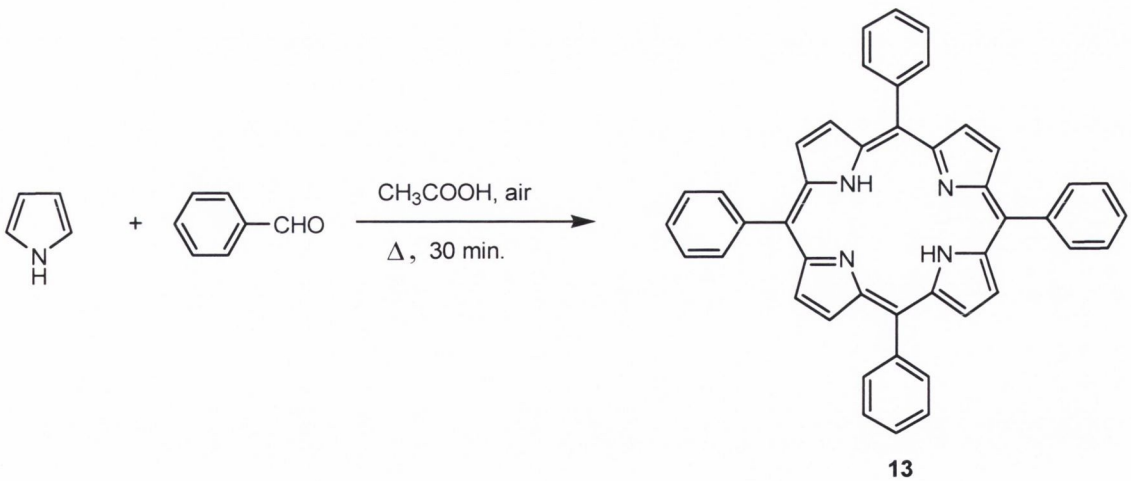
Scheme 1.1. Rothemund method for synthesis of meso-substituted porphyrins.

Calvin and co-workers found that the addition of zinc acetate to the reaction mixture roughly doubled the yield of porphyrin, from 4 — 5 % for tetraphenylporphyrin, H_2(TPP) to 10 — 11 % of the zinc chelate, Zn(II)(TPP).[10] Most applications of the Rothemund method have involved rather robust aryl aldehydes bearing different functional groups like CH_3, OMe, Et_2N, NC, Cl, O_2N in different positions. The temperature used for the synthesis of porphyrins using these aldehydes ranges from 110 °C to 220 °C. Zinc acetate was included in many of the reactions.[11-13] In summary, the features of the Rothemund method are reactions at high concentration and high temperature in the absence of oxidants but the low yield of porphyrin limits its scope of application.

B. Adler Method

Development and mechanistic studies

In 1960, Adler, Longo and co-workers re-examined the synthesis of meso-substituted porphyrins. They performed condensations of benzaldehyde and pyrrole (0.02 M, each) in acetic acid under heating to reflux in glassware open to the atmosphere the presence of a metal salt or benzene containing chloroacetic acid or trifluoroacetic acid (Scheme 1.2).[14] Yields of 30 — 40 % for **13** were obtained with acetic acid or acidified benzene (10 g / 250 mL). This approach is now known as the Adler-Longo method.[15]



13

Scheme 1.2. Adler method for the synthesis of meso-substituted porphyrins, exemplified for H_2(TPP).

The various mechanistic aspects of the reaction of benzaldehyde and pyrrole found by Adler and co-workers are as followed:

(1) The rate of reaction increased with increasing concentration of acetic acid in benzene.

(2) Equimolar ratios of benzaldehyde and pyrrole gave the highest yields.

(3) Reaction under a nitrogen atmosphere resulted in 5 % instead of 35 — 40 % yield.

(4) The reaction was faster in propionic acid than acetic acid but the yield was 20 % rather than 40 %.[16] Propionic acid is most popular due to solubilizing diverse aldehydes.

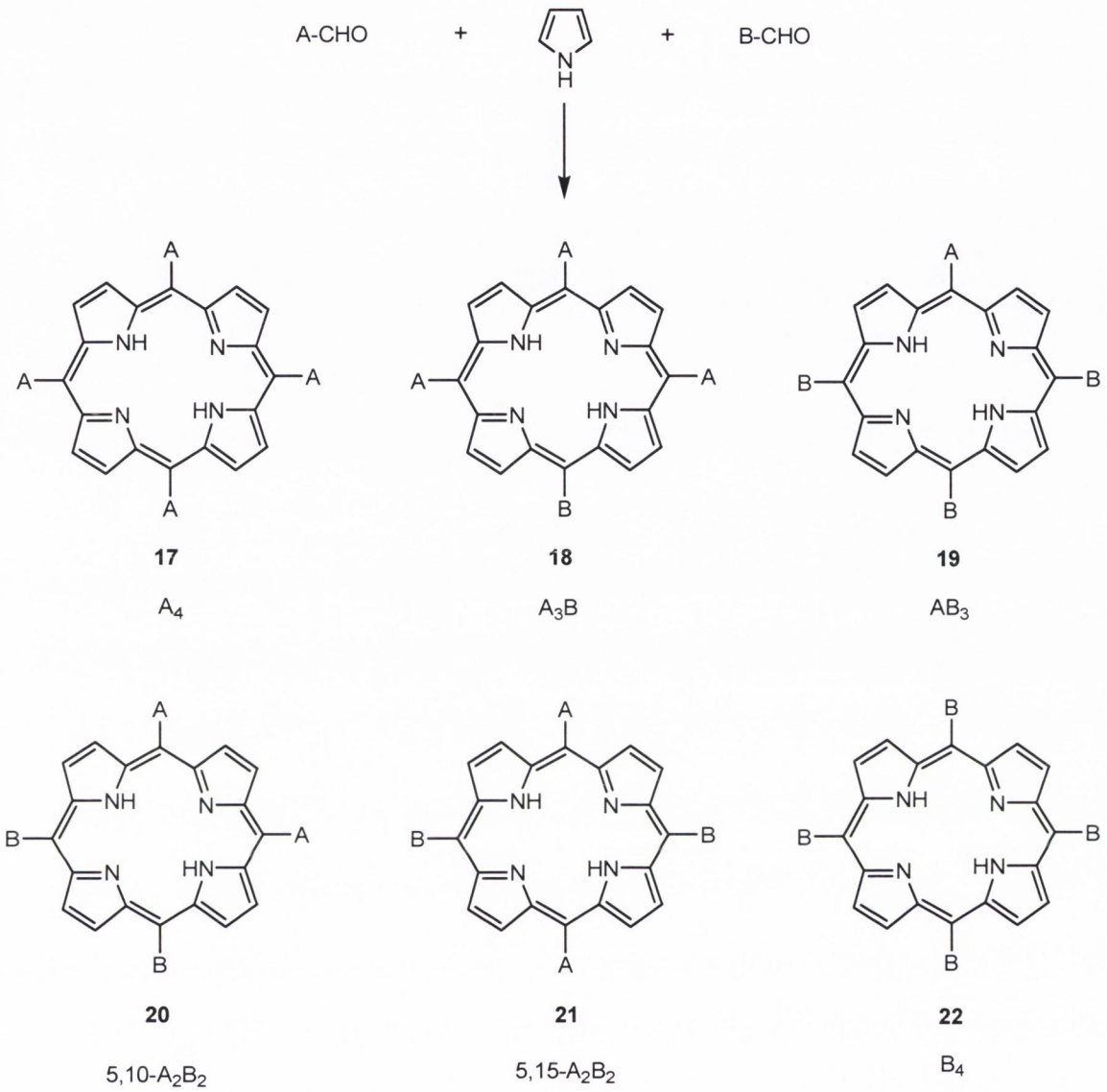
Applications

a) Scope of reaction with various aldehydes

The Adler method was successfully applicable with many aldehydes to afford a variety of meso-substituted porphyrins containing *o*-, *m*- and *p*-aryl substituents of various degree of steric demand. Substituents containing heteroatom clusters, heterocyclic groups and organometallic units have also been synthesized by this method.[17-23]

b) Mixed-aldehyde condensations

While condensation of an aldehyde with pyrrole affords the porphyrin having four identical meso-substituents, many applications call for porphyrins bearing multiple substituents arranged regiospecifically about the porphyrin periphery. One simple approach towards that objective is achieved through a mixed-aldehyde condensation (Scheme 1.3). The reaction of pyrrole with a mixture of two aldehydes affords, in principle, a set of six porphyrins which include the two "parent" porphyrins **17** and **22** (A_4 and B_4) and the four "hybrid" porphyrins **18**, **19**, **20** and **21** (A_3B, AB_3, 5,10-A_2B_2 and 5,15-A_2B_2). This approach of mixed-aldehyde condensation was first used to prepare mono-hydroxy and mono-pyridyl porphyrins[24] and quickly gained acceptance for the preparation of a wide variety of porphyrins bearing two different types of substituents.[19,25] However, the main problem of mixed condensation appears during synthesis of porphyrins bearing different meso-substituents as the number of regioisomers formed is too large. Therefore, the purification and separation workup is too cumbersome.

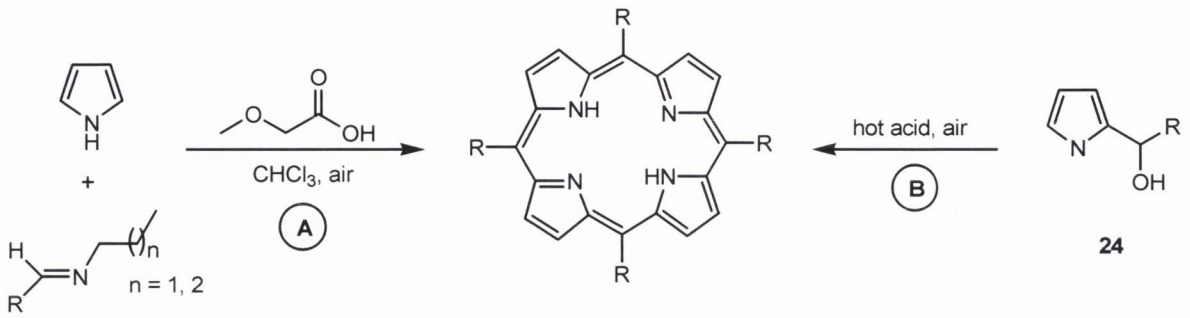


Scheme 1.3. The set of porphyrins formed upon a mixed-aldehyde condensation.

Modifications of Adler method

Pyrrole is known to undergo a Mannich reaction under mild conditions with imines formed from formaldehyde and dialkylamines, affording the α-dialkylaminomethyl derivative.[26,27] Thus, pyrrole and an imine **23** (0.2 M each) were allowed to react for 6 days at room temperature in chloroform containing methoxyacetic acid. After air oxidation, the corresponding porphyrin (**8**, **25**, **26** and **13**) was observed in yields from 7 — 22 % (Scheme 1.4, Route A).

The pyrrole-carbinol **24** is a key intermediate in pyrrole-aldehyde condensation and undergoes self-condensation in hot propionic acid forming the corresponding porphyrins (**27**, **28** and **13**) (Scheme 1.4, Route B).[28]



R (Route **A**)	R (Route **B**)
methyl **8**	**27**
ethyl **25**	**28**
isopropyl **26**	
phenyl **13**	phenyl **13**

Scheme 1.4. One-flask pyrrole-imine condensation (route **A**) and pyrrole-carbinol conversion (route **B**) yielding meso-substituted porphyrins.

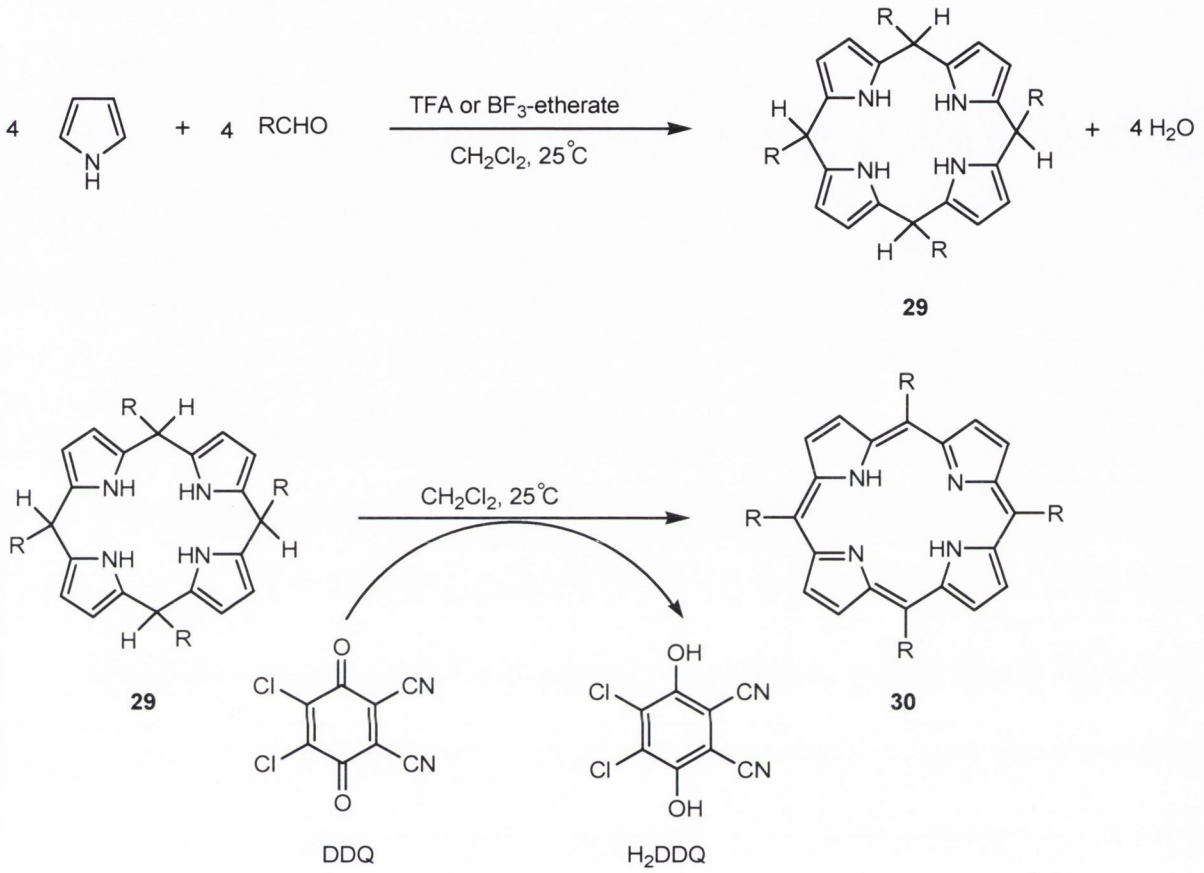
C. Lindsey method (a two-step one-flask room temperature synthesis of porphyrins)

Development

The development of an approach for the synthesis of meso-substituted porphyrins under gentle conditions was motivated by the desire to broaden the scope of available porphyrins model systems. The development of this method was inspired because pyrrole and benzaldehyde are reactive molecules and should not require high temperatures for condensation. The Lindsey method for the synthesis of meso-substituted porphyrins uses a sequential process of condensation and oxidation steps as follows:

A solution of pyrrole and benzaldehyde (10 mM each) in CH_2Cl_2 at room temperature was treated with trifluoroacetic acid or BF_3-etherate. Then, in a second step, a stoichiometric

quantity of DDQ or *p*-chloranil was added, causing conversion at room temperature of the porphyrinogen **29** to the porphyrin **30** in yields 35 — 40 % (Scheme 1.5).[29,30] The method was developed over the period 1979 — 1986.



Scheme 1.5. Two-step one-flask room-temperature synthesis of meso-substituted porphyrins (Lindsey method).

The reaction was found to be quite sensitive to the concentration of the reactants and the acid catalyst. For 10 mM reactants, BF_3-etherate was found to be effective at 1 mM while TFA required a higher concentration of 20 — 50 mM.[30]

Applications

This method has been applied to the synthesis of diverse meso-substituted porphyrins. The overall yields can reach 50 % depending on the aldehyde. The reaction conditions are compatible with a range of *p*-substituted benzaldehydes, *o*-substituted benzaldehydes and benzaldehydes bearing bulky groups at the 3- or 3,5-positions.[31-38] The reaction conditions also are compatible with organometallic units [39], protected sugars[40], heterocyclic aldehydes[41]

and isotopically labelled aldehydes.[42] The Lindsey method has been also successfully applied to the preparation of porphyrins bearing two different types of meso-substituents *via* a mixed-aldehyde condensation using two different aldehydes bearing alkyl chains and aromatic groups with various substituents in different positions.[43-47]

1.3.4 Routes to specific classes of meso-substituted porphyrins

A. 5,15-Substituted porphyrins

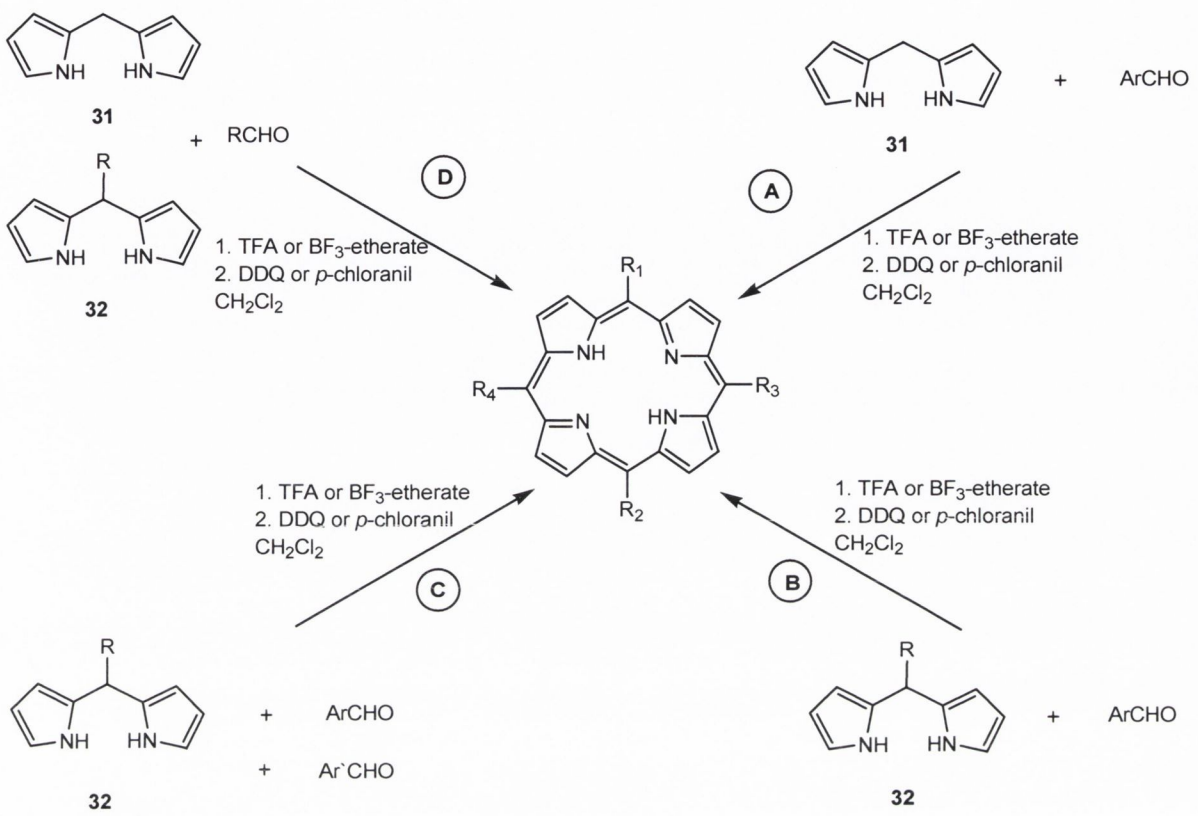
Porphyrins bearing substituents in the 5,15-positions are useful for diverse applications. The mixed-aldehyde condensation affords 5,15-substituted porphyrins in 12.5 % of the total porphyrins (based on 1:1 ratio of the two aldehydes). From the same reaction, the 5,10-substituted porphyrin is isolated in 25 % yield. As the 5,10- and 5,15- substituted porphyrins bear two of the same substituents, separation by adsorption chromatography is often difficult. Rational syntheses of 5,15-substituted porphyrins have been developed based on the MacDonald [2 + 2] condensation of a dipyrromethane and an aldehyde, as shown in Scheme 1.6 (Routes A to D) as follows:

Route A: Reaction of meso-unsubstituted, *β*-unsubstituted dipyrromethanes **31** with a wide variety of aryl aldehydes at room temperature over 15 h in CH_2Cl_2 containing trifluoroacetic acid. Subsequent oxidation with DDQ or *p*-chloranil affords the corresponding 5,15-substituted porphyrins **33** in 73 — 92 % yields.[48]

Route B: Reaction of meso-substituted, *β*-unsubstituted dipyrromethanes **32** with a wide variety of aryl aldehydes under the same reaction conditions to afford *trans*-A_2B_2 meso-substituted porphyrins **34**.[49-51]

Route C: Reaction of meso-substituted, *β*-unsubstituted dipyrromethanes **32** with two different aldehydes to afford A_2BC-type meso-substituted porphyrins **35**. The chromatographic separation must be done for the desired A_2BC-porphyrin.[52]

Route D: Reaction of meso-unsubstituted, *β*-unsubstituted dipyrromethanes **31** and meso-substituted, *β*-unsubstituted dipyrromethanes **32** with an aldehyde to afford a porphyrin **36** with one free meso-position.[53]

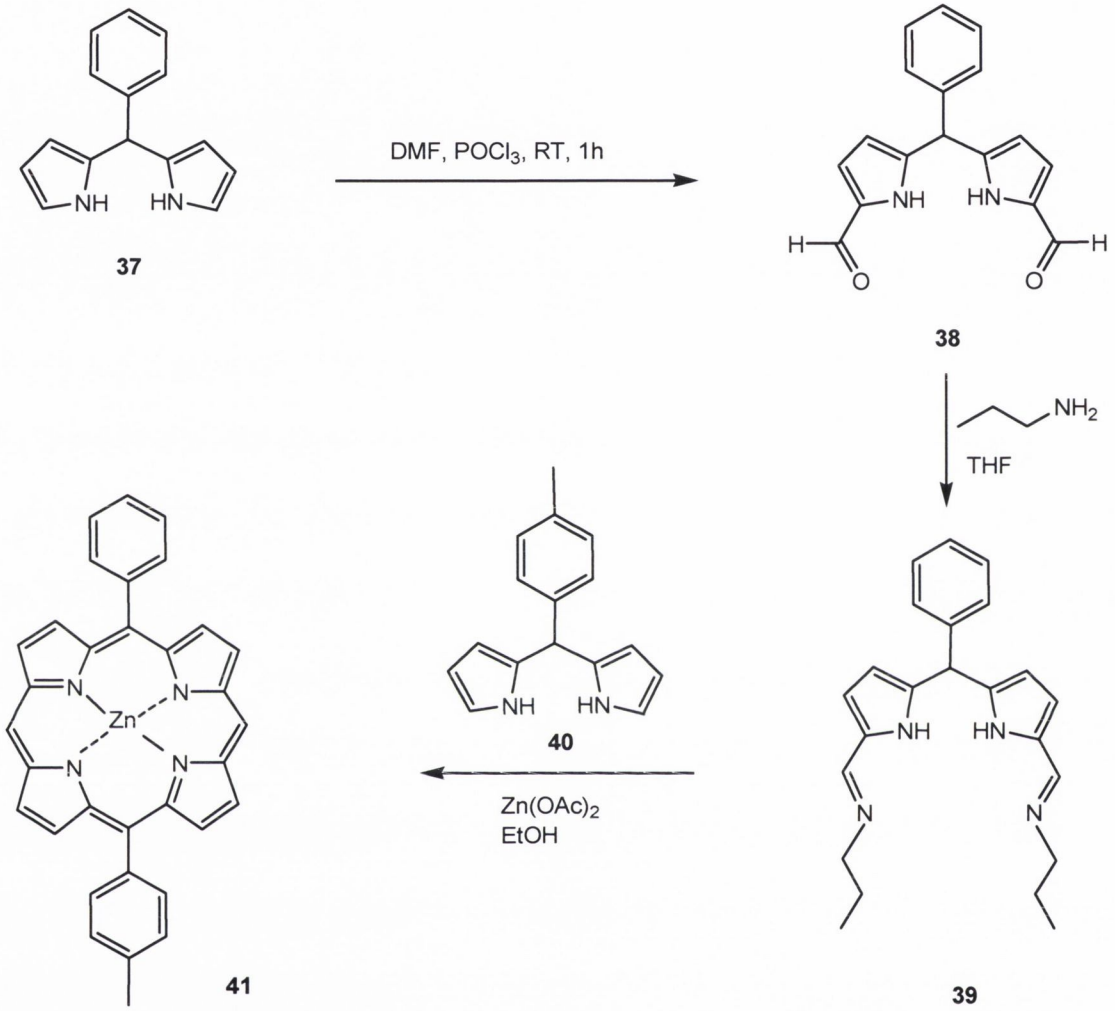


Route	Compound formed
A	**33** : $R_1 = R_2 = Ar$, $R_3 = R_4 = H$
B	**34** : $R_1 = R_2 = Ar$, $R_3 = R_4 = R$
C	**35** : $R_1 = Ar$, $R_2 = Ar`$, $R_3 = R_4 = R$
D	**36** : $R_1 = R_2 = R_3 = R$, $R_4 = H$

Scheme 1.6. Routes (A to D) for different classes of 5,15-substituted porphyrins using dipyrromethane.

In 2005, Lindsey and co-workers developed a new synthesis of 5,15-AB-porphyrins which are valuable compounds in bioorganic and materials chemistry. Their synthesis employs 1,9-diformylation of dipyrromethane, conversion of the diformyldipyrromethane to the bis(imino) derivative, and reaction of the bis(imino)dipyrromethane with a dipyrromethane in presence of zinc acetate to give the zinc-porphyrin bearing 5,15-AB-substituents. Scheme 1.7 illustrates the synthetic approach to the AB-porphyrin **41** which includes 1,9-diformylation of phenyl-dipyrromethane **37** *via* Vilsmeier reaction to form 1,9-diformyldipyrromethane derivative **38**. Imination was achieved by treatment of **38** with *n*-propylamine at room temperature to afford

1,9-bis(imino)dipyrromethane **39** which reacted with a dipyrromethane **40** substituted with tolyl group over 2 h in refluxing ethanol containing zinc acetate to form zinc-porphyrin with 5,15-AB-substituents **41** in yields of 30 — 45 % depending on the reaction conditions.[54]



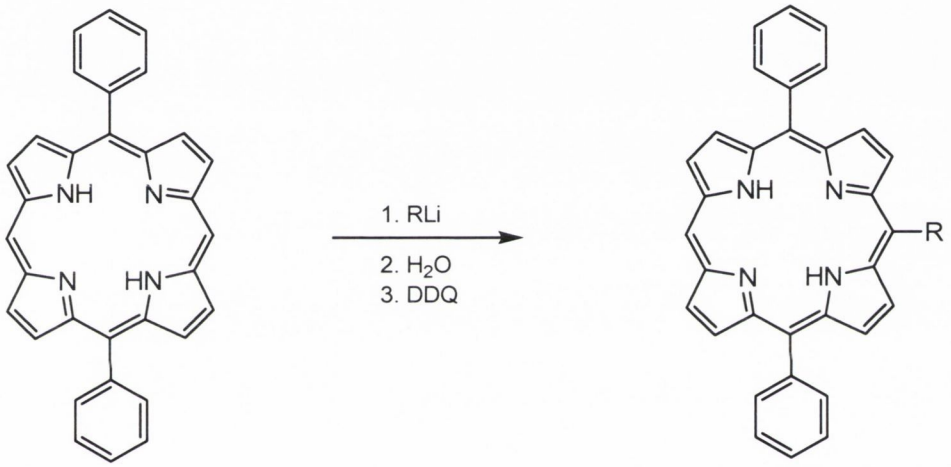
Scheme 1.7. An example for the Lindsey synthesis of 5,15-AB-substituted porphyrins via imine-substituted dipyrromethanes.

B. meso-Substituted porphyrins using organolithium reagents

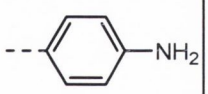
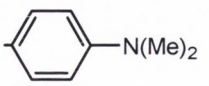
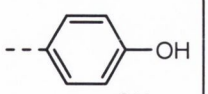
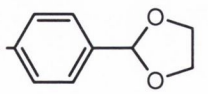
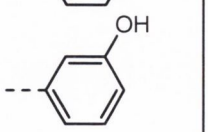
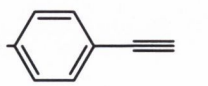
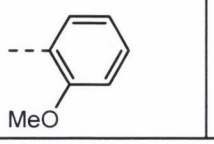
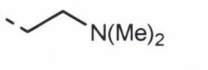
Senge and co-workers found that porphyrins readily undergo meso-substitution reactions with organolithium reagents and since then, they have developed this reaction to be a generally applicable method for the preparative synthesis of functionalized unsymmetric porphyrin precursors.[55-61] As porphyrins have broad medicinal applications in photodynamic therapy (PDT), further development of these applications may be enhanced by unsymmetric and

highly functionalized compounds. Thus, functionalized unsymmetric porphyrin precursors should be key intermediates for the required compounds.

The functionalized porphyrins **43-50** were synthesized in good yields (~80 %) except for **45** through the reaction of organolithium reagents with 5,15-diphenylporphyrin **42** followed by hydrolysis with water and subsequent oxidation with DDQ (Scheme 1.8).[62] In order to achieve high yields in the synthesis shown in Scheme 1.8, 10 — 15 equivalents of organolithium reagents were used. Indeed, the A_2B-type meso-substituted porphyrins **43-50** bearing NH_2, -OH, -OMe, $-N(Me)_2$, *p*-ethynyl and 1,3-dioxolan-2-yl groups which are highly reactive centers could be prepared easily.[62]



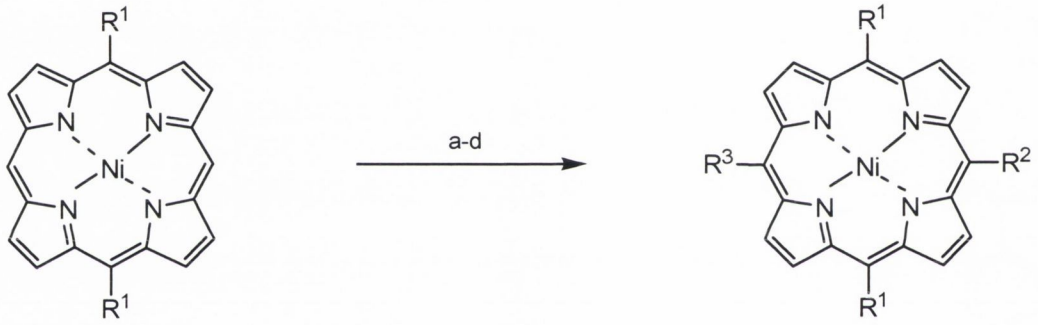
42 **43-50**

R	Yield (%)	R	Yield (%)
43 	82	**47** 	78
44 	75	**48** 	86
45 	30	**49** 	85
46 	83	**50** 	75

Scheme 1.8. Synthesis of functionalized unsymmetric porphyrins by using organolithium reagents.

Senge and Feng also found that reaction of (5,15-dibutyl/phenylporphyrinato)nickel(II) **51** and **52** with R^2Li under anhydrous conditions affords 5,10,15-trisubstituted porphyrin anions that can be used as *in situ* nucleophiles for reaction with electrophilic reagents such as alkyliodides. After oxidation with atmospheric oxygen, the 5,10,15,20-tetrasubstituted A_2BC-type porphyrins **53-61** were obtained in yields from 50 to 90 % (Scheme 1.9).[63] The reaction sequence was addition of RLi, hydrolysis with water, addition of RI, and subsequent oxidation with air which is considered as a two-step one-pot reaction. Scheme 1.9 also shows the use of alkyl iodide reagents with functional groups such as –I, -OH, -Br, -COOR, and –CN.

The use of the respective free base porphyrin under similar reaction conditions gave 5,10,15-trisubstituted porphyrins as the sole product, similar to the standard reaction sequence (porphyrin, RLi, H_2O and DDQ) without using of alkyliodide.



51 : R^1 = Ph
52 : R^1 = *n*Bu

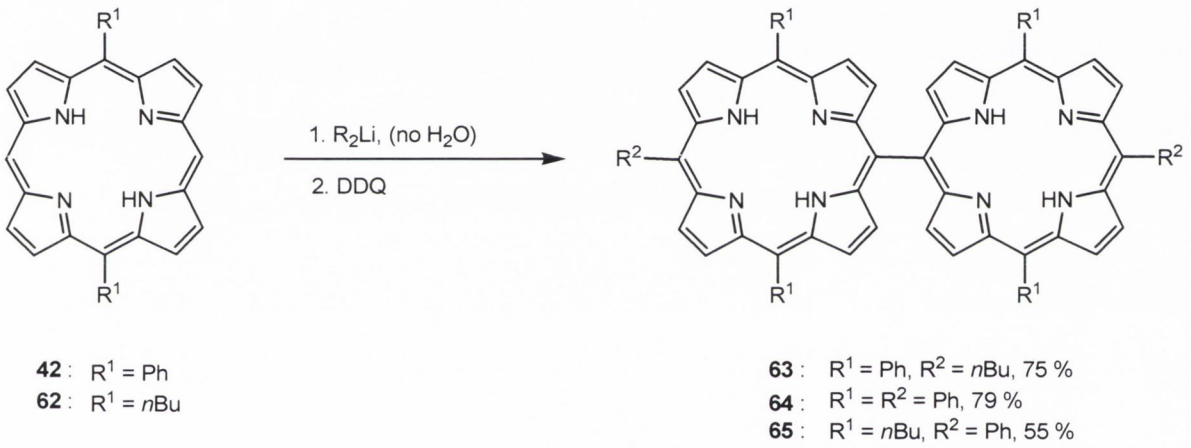
53-61

	R^1	R^2	R^3	Yield(%)
53	Ph	*n*Bu	*n*Bu	92
54	Ph	Ph	*n*Bu	90
55	Ph	*n*Bu	$CH_2CH_2CH_2CH_2I$	79
56	Ph	Ph	$CH_2CH_2CH_2CH_2I$	71
57	Ph	*n*Bu	$CH_2CH_2CH_2CH_2OH$	48
58	Ph	Ph	$CH_2CH_2CH_2COOEt$	52
59	Ph	Ph	$CH_2CH_2CH_2CN$	80
60	*n*Bu	Ph	$CH_2CH_2CH_2CN$	62
61	Ph	Ph	$CH_2CH_2CH_2CH_2Br$	24

Reagents and conditions: (a) R^2Li, THF, -70 ; (b) H_2O; (c) R^3I, 60 min, room temperature; (d) air.

Scheme 1.9. One-pot, two-step reaction of 5,15-disubstituted porphyrins with R^2Li/R^3I.

Some useful synthetic variations were also possible with free-base porphyrins. One example is the preparation of directly meso-meso linked bisporphyrins (Scheme 1.10).[64] Reaction of 5,15-disubstituted free-base porphyrins **42** or **62** with RLi under anhydrous conditions afforded 5,10,15-trisubstituted porphyrin anions followed by oxidation with DDQ, the bisporphyrins **63-65** were accessible in good yields. The mechanistic investigations of this reaction indicated that simple omission of the hydrolysis step allowed the facile preparation of 5,5'-linked bisporphyrins *via* direct oxidation of the anion to a π-stabilized radical followed by radical dimerization.



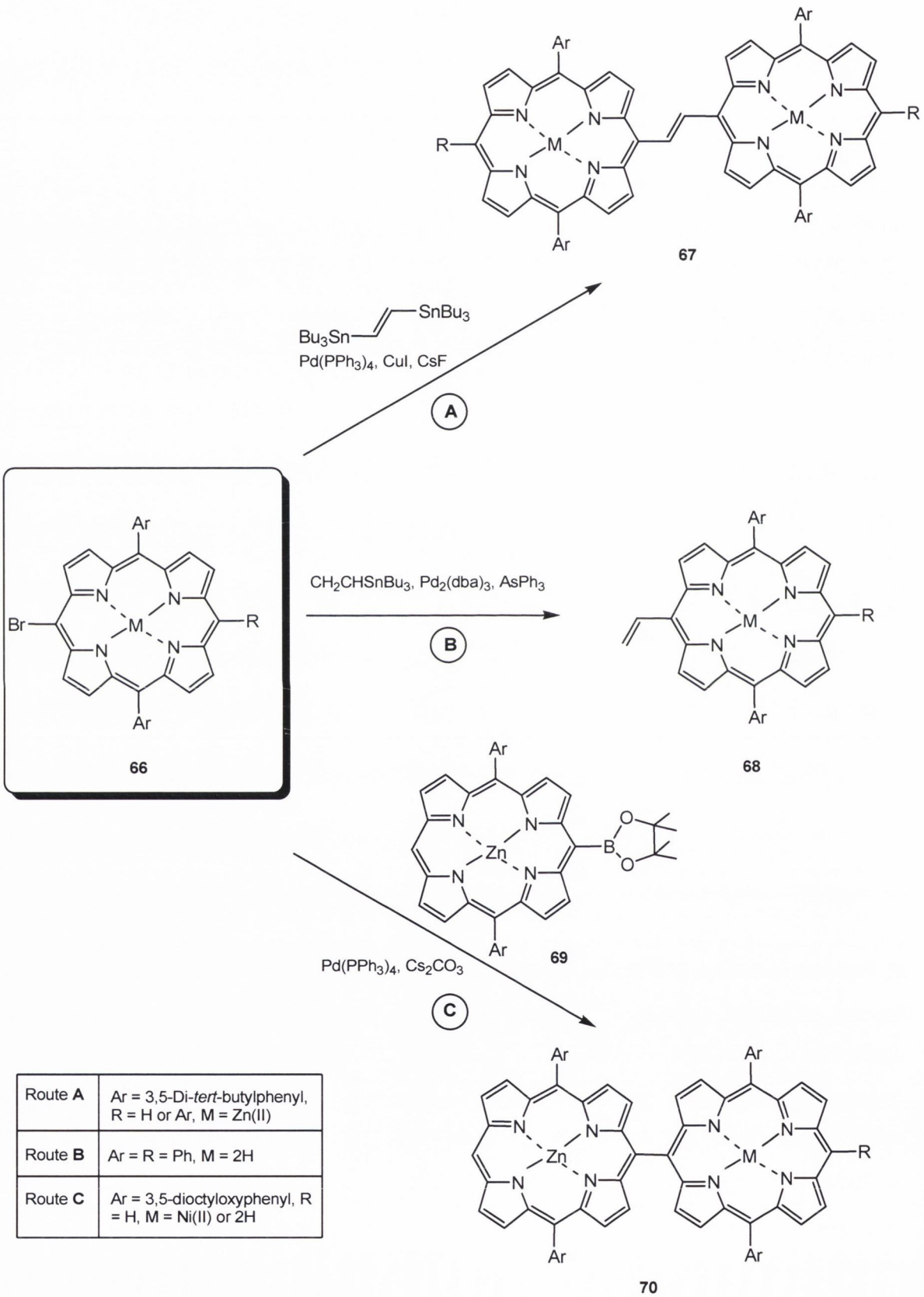
42 : R^1 = Ph
62 : R^1 = *n*Bu

63 : R^1 = Ph, R^2 = *n*Bu, 75 %
64 : R^1 = R^2 = Ph, 79 %
65 : R^1 = *n*Bu, R^2 = Ph, 55 %

Scheme 1.10. Synthesis of the meso-meso linked bisporphyrins using 5,15-disubstituted free base porphyrins and organolithium reagents in absence of water.

C. Palladium-catalyzed coupling and fuctionalizing the meso position of porphyrins

Several coupling reactions have been reported for the functionalization and linking of porphyrins using palladium catalysis.[44,65-67] Scheme 1.11 shows three different approaches for coupling and functionalizing the meso position of porphyrins using meso-bromoporphyrin **66** and palladium catalysis. Palladium catalysed Stille coupling of bromoporphyrin **66** with bis(tributylstannyl)ethene using $Pd(PPh_3)_4$, CuI and CsF gave meso-meso vinylene linked porphyrin dimers **67** in yields 44 % (R = H) and 58 % (R = Ar) (Scheme 1.11, Route A).[65] An example for functionalization of a porphyrin is illustrated in Scheme 1.11, Route B. Reaction of bromoporphyrin **66** with tri-*n*-butyl(vinyl)tin in the presence of tris(dibenzylideneacetone)dipalladium(0) and $AsPh_3$ in dry THF afforded porphyrin **68** in



Route **A**	Ar = 3,5-Di-*tert*-butylphenyl, R = H or Ar, M = Zn(II)
Route **B**	Ar = R = Ph, M = 2H
Route **C**	Ar = 3,5-dioctyloxyphenyl, R = H, M = Ni(II) or 2H

Scheme 1.11. Exemplary routes to the functionalization and linking of porphyrins using various Pd catalysts.

88 % yield.[66] Route C in Scheme 1.11 shows a Pd-catalyzed coupling for the synthesis of meso-meso coupled porphyrin arrays. Coupling of porphyrin boronate **69** and meso-bromoporphyrin **66** was carried out in a mixture of toluene and DMF in presence of $Pd(PPh_3)_4$ and Cs_2CO_3 at 80 °C to gave **70** in 62 % yield.[67]

D. Porphyrins bearing four different meso-substituents (ABCD-porphyrins)

The synthesis of ABCD-porphyrin **71** has recently seen significant developments. Retrosynthetic analysis shows several ways in which the synthesis of ABCD-porphyrins can be approached (Figure 1.4)[68] which are summarized as followed: The MacDonald-type [2 + 2] condensation which employes dipyrromethanes **72** and **73** directly, [3 + 1] condensation of tripyrrane **74** and pyrrole or mixed condensation of four different aldehydes and pyrrole.[7,69] In addition, ABCD-porphyrins can also be formed *via* cyclization of hydroxymethylbilane **75** or bilane **78** and aldehyde condensation.[70,71] Recently, an ABCD-porphyrin **71** has been formed by using A-type porphyrins **76** with three different organolithium reagents *via* three steps.[72]
The synthesis of meso-substituted porphyrins from dipyrromethane intermediates requires introducing substituents at the α and α'-positions (2- and 5- positions) of the pyrrole nucleus. Introducing acyl groups is ideal, since pyrrole readily undergoes electrophilic aromatic substitution.[68] An α-substituted pyrrole can be acylated at the α'-positions as long as the α-substituent is not electron-withdrawing.[73] This means that introduction of groups at the α and α'-positions must involve electron-releasing groups preceding electron-withdrawing groups in order to lead to introduce the second acyl group to the 5-position rather than the 4-position.[73]
Dipyrromethane plays an important role in the MacDonald-type [2 + 2] condensation and in preparation of tripyrranes, bilanes, or higher oligomeric pyrroles. Indeed, the dipyrromethanes are relatively stable compounds. This has prompted some research groups to investigate methods for functionalizing dipyrromethanes such as they can be used in rational syntheses of ABCD-porphyrins. Smith and co-workers described a synthesis of ABCD-porphyrins involving the acid-catalyzed condensation of two different dipyrromethanes in refluxing propionic acid.[74,75] Ogoshi`s group synthesized an ABCD-porphyrin in a similar manner.[76,77]
Synthetic approaches to pure ABCD-porphyrins are currently under development by Lindsey`s group.[68,78-80] Scheme 1.12 shows an example of the synthesis of porphyrins bearing four different meso-substituents. Reaction of *o*-mercaptophenol **79** with a *p*-methyl-benzoic acid **80**

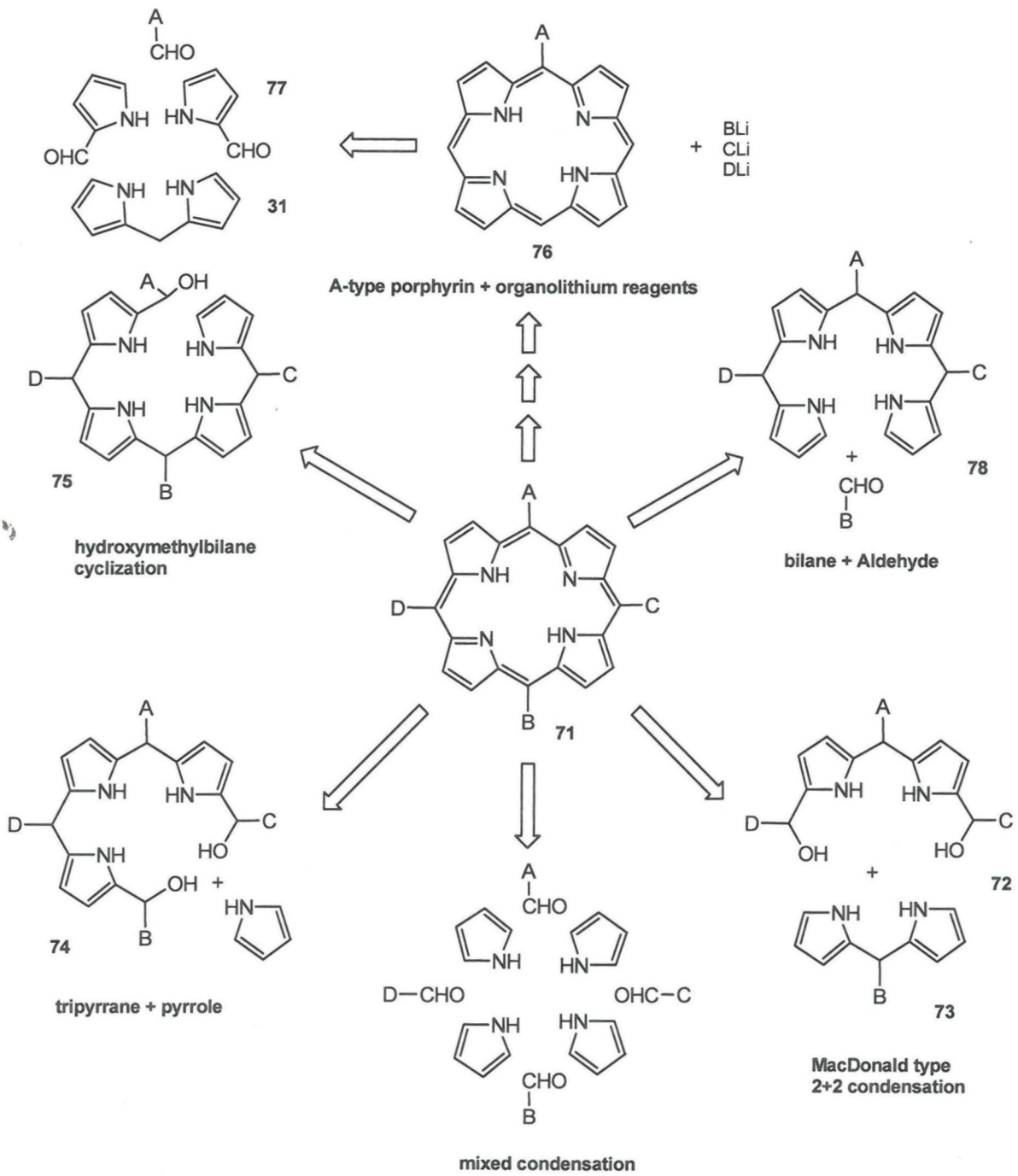
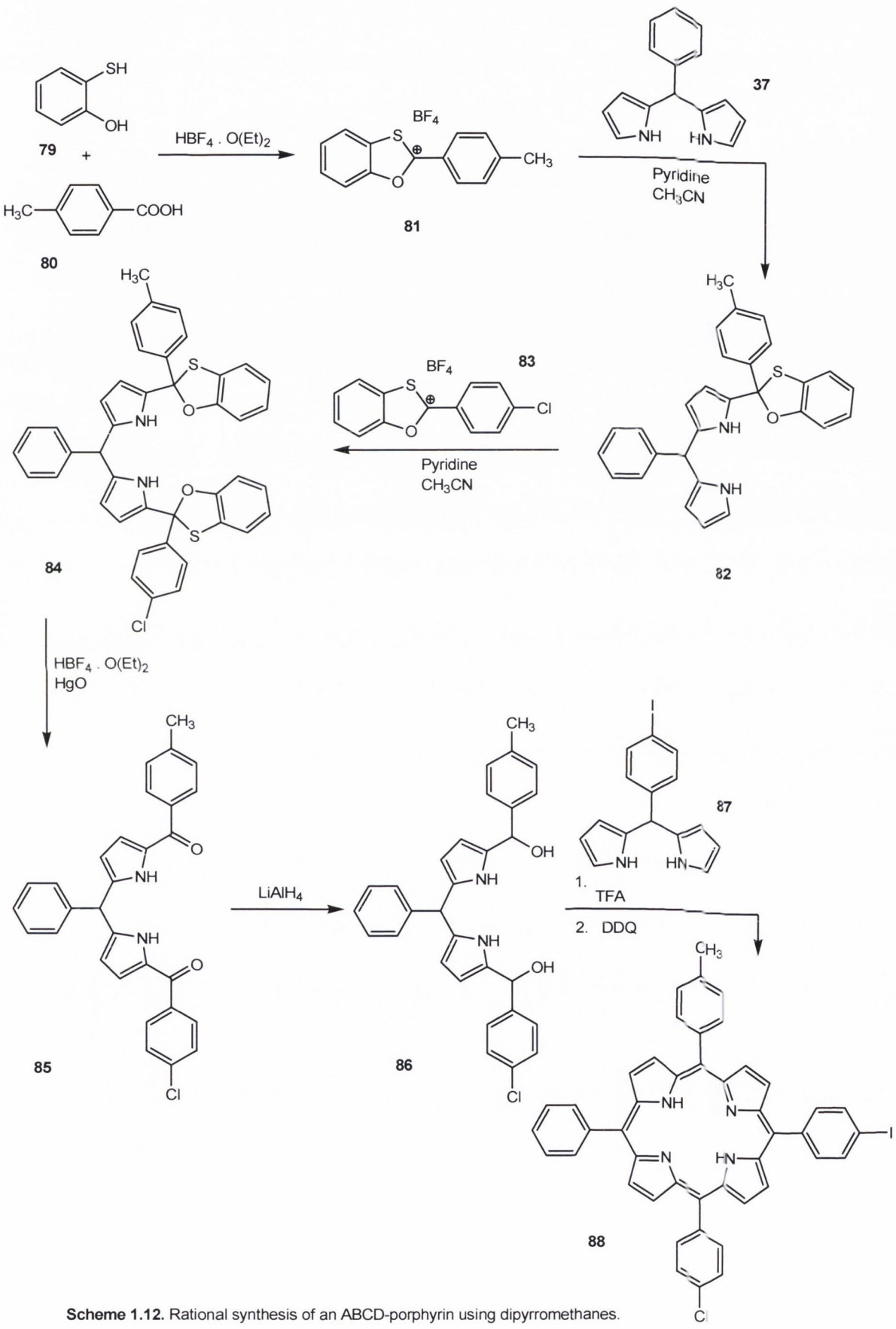


Figure 1.4. Retrosynthetic analysis for ABCD-porphyrins.

in the presence of HBF_4-etherate gave the benzoxathiolium tetrafluoroborate **81**, a masked acyl equivalent, which reacted with dipyrromethane **37** at room temperature to afford the mono-alkylated dipyrromethane **82** in 67 %. Treatment with a second benzoxathiolium tetrafluoroborate **83** gave the 1,9-dialkylated dipyrromethane **84** in quantitative yield. Oxidative hydrolysis yielded the 1,9-diacyl dipyrromethane **85**, a stable crystalline compound.



Scheme 1.12. Rational synthesis of an ABCD-porphyrin using dipyrromethanes.

Reduction of **85** with $LiAlH_4$ gave the bis-carbinol **86** which was used in conjunction with a second dipyrromethane **87** in a [2 + 2] condensation, giving the regioisomerically pure ABCD-porphyrin **88**. All the steps in this synthesis gave high yields except the final [2 + 2] condensation, which proceeded only in 13 % yield.[68]

1.4 Applications of porphyrins in photodynamic therapy (PDT)

1.4.1 The concept of photodynamic therapy

Photodynamic therapy (PDT) is a promising modality for the treatment of cancer.[81-84] In PDT, light, O_2, and a photosensitizing drug are combined to produce a selective therapeutic effect. PDT is a selective treatment modality that affects mainly the target tissue. The selectivity is based on a difference in the photosensitizer concentration between normal and target tissues and on the directing of light into the target tissues. The concept of photodynamic therapy as in Figure 1.5[85] is simple: (1) Intravenous injection of the photosensitizer into the blood stream. (2) After injection, the photosensitizer accumulates in the target tissue during 3 — 96 h, depending on the photosensitizer used. (3) After the accumulation period, light directed to the tissue activates the photosensitizer and, in the presence of ground-state (triplet) oxygen ($^3O_2$), reactive singlet oxygen species are formed. (4) Damage to vital structures and functions of cells as a result of singlet oxygen, causes tumour tissue destruction.[86,87]

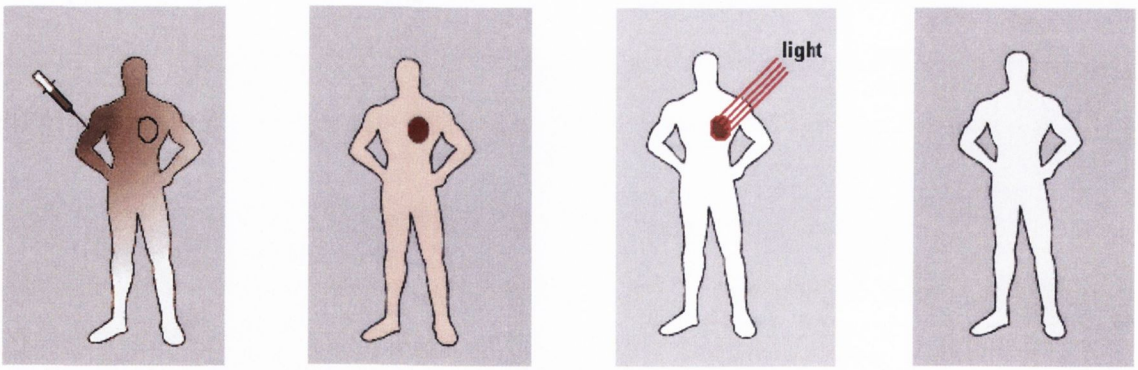


Figure 1.5. Illustrative pictures for the stages of photodynamic therapy on a patient: (1) The drug photosensitizer is given by injection. (2) After some time the photosensitizer concentrates in the tumour. (3) The photosensitizer is activated by light. (4) The tumour is selectively destroyed.[85]

Porphyrins have been found to be good candidates for photosensitizers in PDT. As porphyrins are cyclic conjugated electronic structures, they can absorb energy from light and transfer it to molecular oxygen. Toxic oxygen species such as singlet oxygen and free radicals are thus formed. Indeed, these species are very reactive and can damage proteins, lipids, nucleic acids and cellular components.

1.4.2 Mechanism of photodynamic therapy

Singlet oxygen generated in the cells can be explained using simple photophysics.[88,89] Figure 1.6 shows a simplified Jablonski diagram (with vibrational levels omitted). Provided that the porphyrin possesses an absorption maximum at a wavelength corresponding to that of the incident laser light, shining light on a highly colored porphyrin causes excitation to the singlet excited state ($^1P^*$). The singlet excited porphyrin can decay back to the ground state with release of energy in the form of fluorescence - enabling identification of tumor tissue. If the singlet state lifetime is suitable (and this is the case for many porphyrins) it is possible for the singlet state to be converted into the triplet excited state ($^3P^*$) which is able to transfer energy to another triplet state. One of the very few molecules with a triplet ground state is dioxygen, which is found in most cells. Energy transfer therefore takes place to afford highly toxic singlet oxygen ($^1O_2$) from ground state dioxygen in the triplet state ($^3O_2$), provided the energy of the $^3P^*$ molecule is higher than that of the product $^1O_2$.

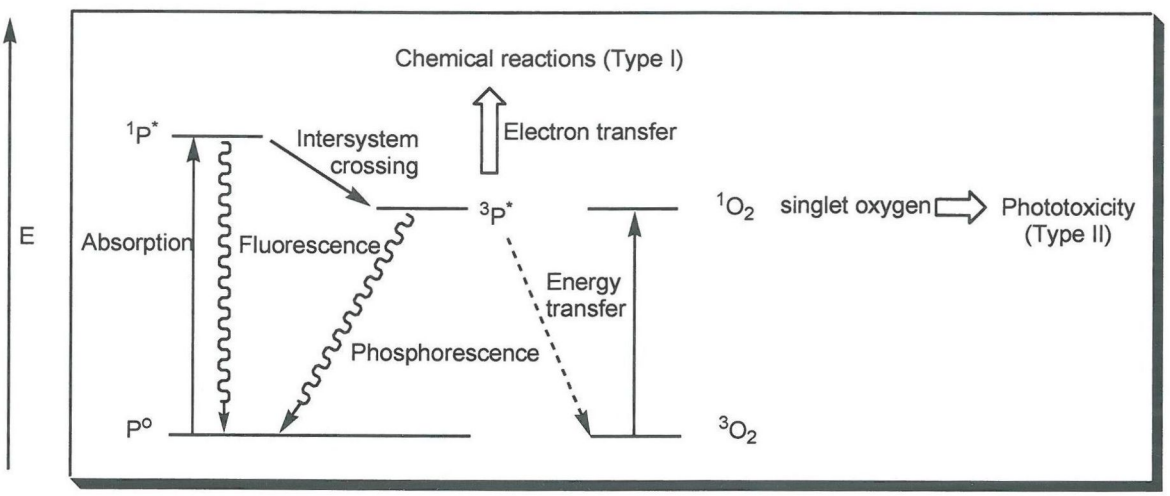


Figure 1.6. A simplified Jablonski diagram for PDT.

Photochemical reactions involved in PDT

Triplet photosensitizers can undergo either Type I reaction (electron or hydrogen atom transfer); through interaction with substrate or solvent, or Type II reaction (energy transfer); through interaction with molecular oxygen.[90] These two photochemical reactions are shown in Figure 1.7. Transfer of energy to molecular oxygen (type II) is thought to be the primary photochemical reaction in porphyrin-mediated PDT. This results in the *in situ* generation of singlet oxygen ($^1O_2$). Electron transfer from the sensitizer to oxygen may also occur in some cases, giving oxidized sensitizer and superoxide anions (Figure 1.7).

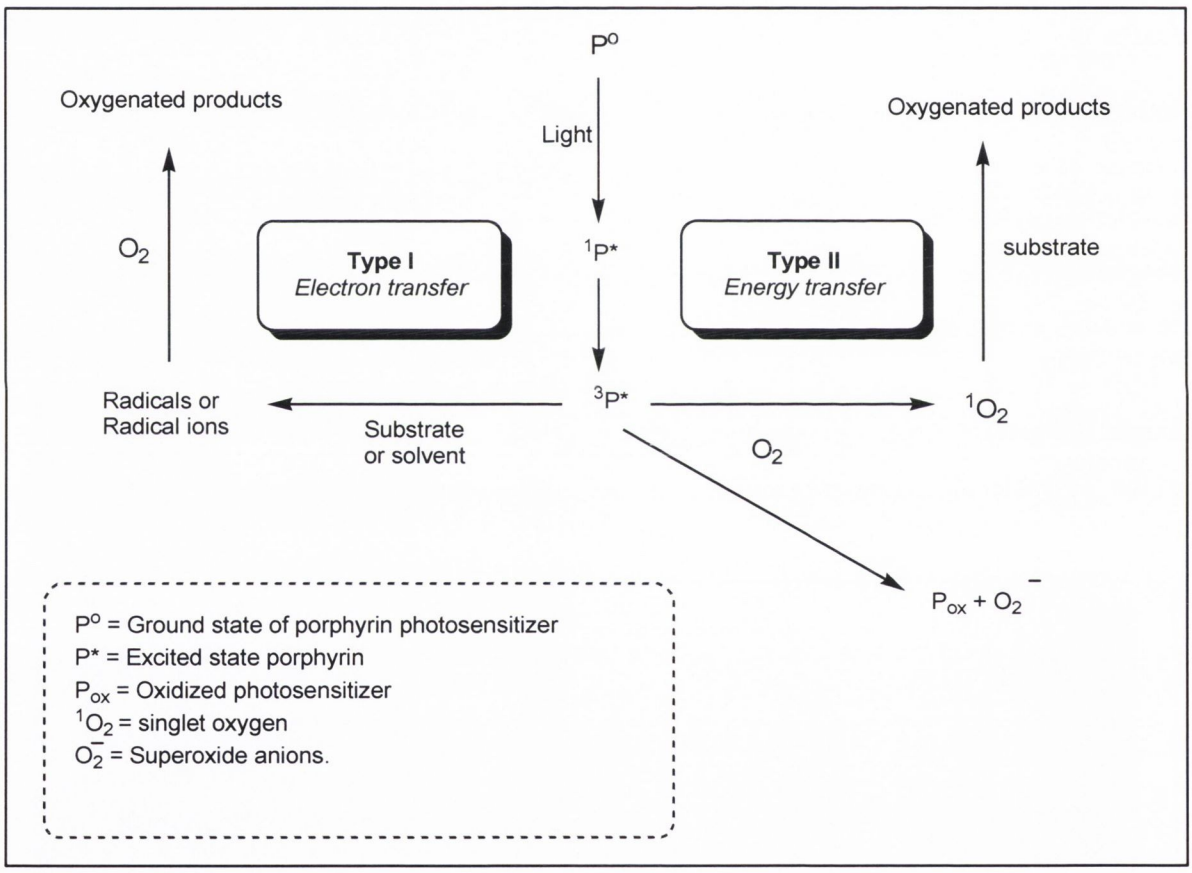


Figure 1.7. Type I and Type II photochemical reactions in PDT.

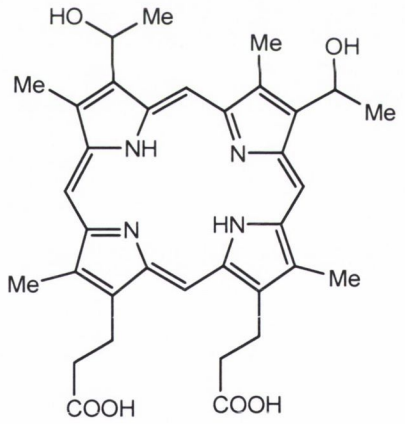
1.4.3 Properties of good photosensitizer

The crucial part in the PDT process relies on the molecular features of the photosensitizer.[88,91] The structural features of an efficient photosensitizer should be an amphiphilic character through insertion of functional groups with different polarities, tunable modification of the

conjugated π-system and synthesized in high yields and in few steps. For the treatment of cancer, the ideal photosensitizer should meet the following requirements:
(1) be chemically pure and have known composition; (2) be nontoxic in the absence of light; (3) be preferentially retained by the target tissue; (4) absorb light of sufficiently long wavelengths (600 — 800 nm) so that the therapeutic effect of PDT would be as deep as possible and that the light used would not cause photosensitization of healthy tissues; (5) have a high quantum yield of singlet oxygen; (6) be easily administrated, orally, topically or intravenously; (7) be rapidly excreted from the body to provide low systemic toxicity.

1.4.4 Porphyrin photosensitizer structures

Most photosensitizers used in PDT are cyclic tetrapyrroles, comprising substituted derivatives of porphyrin, chlorin, and bacteriochlorin. The first photosensitizers most commonly used in PDT were hematoporphyrin (Hp) (Figure 1.8., **89**) and hematoporphyrin derivatives (HpD) during the period from 1961 to 1983. Hence, these tetrapyrroles comprised the first generation photosensitizer. [86]



89

Figure 1.8. Hematoporphyrin as the first generation photosensitizer.

HpD was the first photosensitizer to receive regulatory approval in Canada in 1993 and has received subsequent approval in the U.S., Europe, and Japan for treatment of several types of cancer.[92] However, the limitation of HpD is that it is a mixture of compounds that include the hematoporphyrin monomer, dimer, and oligomers.[93] Partial purification of this mixture gives the commercial form, Photofrin®.[94] This purified product still consists of many porphyrin containing compounds which creates difficulties in their manufacture. The absorption

spectrum (so-called etiotype spectrum) of HpD is similar to that of Photofrin®. It contains the strong Soret band, typical for porphyrins, at about 400 nm and the Q-bands of lower intensity at 500, 540, 570, and 630 nm. HpD`s absorption at 630 nm allows light to penetrate reasonably deep into tissues.[95]

The absorption of red light by porphyrins can be strengthened and shifted to longer wavelengths with suitable substituents in the meso-positions. 5,10,15,20-Tetra(3-hydroxyphenyl)porphyrin (*m*-THPP) (Figure 1.9, **90**) and 5,10,15,20-tetra(4-sulfonatophenyl)porphyrin (*p*-$TPPS_4$) (Figure 1.9, **91**) are substituted porphyrins developed as potential new photosensitizers for PDT. *m*-THPP is 25 — 30 times as effective as HpD or Photofrin® as a photosensitizer.[96]

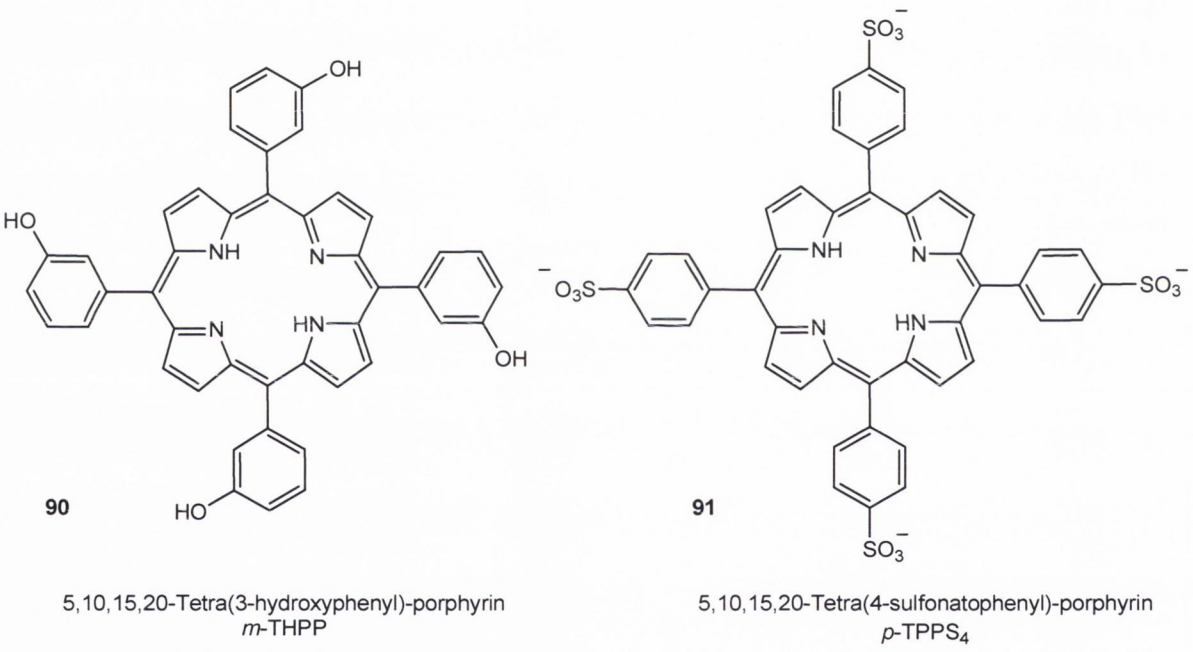


Figure 1.9. meso-Substituted porphyrins that have been developed as potential photosensitizers for PDT.

Finally, PDT has many advantages as compared to the traditional cancer treatments (cytostatic chemotherapy, radiation, and surgery)[88,97] which are summarized as followed: (1) It is a selective treatment that does not destroy healthy tissues. (2) It is an effective treatment as it's easy and fast. (3) There are no serious side effects and no resistance normally develops. (4) It can be used to treat many different kinds of cancers, including cancers resistant to other forms

of treatment. (5) Most porphyrins photosensitizers are fluorophores, so they can also be used in tumor detection and in establishing the tumor size and location before PDT.

1.5 Strategy

The research undertaken in the present study will include the synthesis of functionalized unsymmetrically substituted porphyrins for potential applications in photodynamic therapy. Chapter 2 will study the synthesis of novel A_2BC-porphyrins bearing highly reactive centers in substituents at the meso positions using corresponding functionalized organolithium reagents *via* two-step reactions.

The main focus of Chapter 3 will be on one-pot synthesis of A_2BC-porphyrins with different functional groups in the meso-positions using functionalized organolithium reagent and different alkyl/aryl iodides. The reaction mechanism of A_2BC-porphyrin formation is also postulated.

Chapter 4 will discuss the one-pot synthesis of ABCD-porphyrins with different functional groups in the meso-positions using functionalized organolithium reagent and different alkyl/aryl iodides. In addition, synthesis of ABCD-porphyrins *via* two-step reactions will be also reported. New ABC-porphyrins are also formed during ABCD-porphyrins synthesis and these will be also reported.

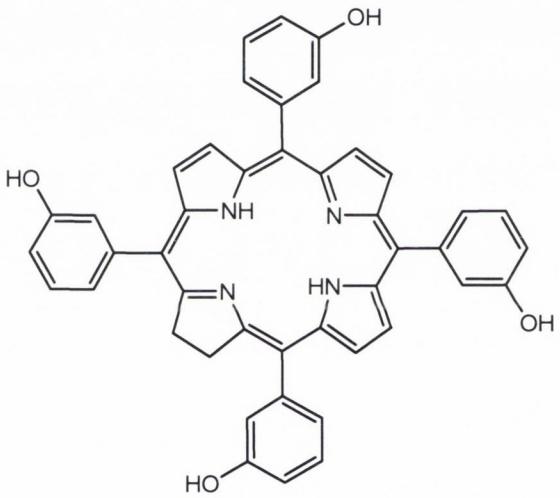
Chapter 5 will be concerned with the synthesis of novel chlorins *via* reaction of functionalized A_4-porphyrins with different organolithium reagents. Electronic effect of the functional groups in the A_4-porphyrins and the steric effect of the organolithium reagents were also examined.

Chapter 2

Synthesis of new functionalized A_2BC-porphyrins as potential lead structures for applications in photodynamic therapy (PDT)

2.1 Introduction

As explained in Chapter 1, substituted tetrapyrrolic systems have broad applications in the area of medicinal treatment of tumors by photodynamic therapy (PDT). Numerous substances have been tested for their suitability as photosensitizers but till now only few photosensitizers have gained approval of the legal authorities in Europe and the United States, namely Photofrin®, Verteporfin® (benzoporphyrin derivative), ALA-PpIX (δ-aminolevulinic acid-induced protoporphyrin IX and Temoporfin **92** (*m*-THPC) [5,10,15,20-tetra(3-hydroxyphenyl)chlorin] (Figure 2.1).[98-100]



92

Figure 2.1. Structure of Temoporfin.

The amphiphilic structure is an important additional property as the molecular frameworks often have hydrophilic and hydrophobic parts. This amphiphilicity has been identified as an important target for facilitating the localization of the photosensitizers in tumor cells. It is important for the photosensitizer to be hydrophilic in order to be easily administered systemically *via* injection into the bloodstream which is water-based system. However, the photosensitizer must also be ideally hydrophobic in order to be able to get into cells by traversing lipid membranes. Very strongly hydrophilic photosensitizers have been shown to lack high PDT efficacy, most probably due to the fact that the singlet oxygen is generated in an aqueous environment, too far away from sensitive cellular structures.[101]

Thus, for developing new photosensitizers for PDT, the target should be a series of compounds differing in the extent of hydrophilic/hydrophobic substitution. This will allow a systematic assessment of membrane affinity to establish quantitative structure activity relationships (QSAR). Therefore, so-called amphiphilic molecules as potential photosensitizers are a prime target in this project. This will involve the synthesis of unsymmetric tetrapyrrolic systems with mixed hydrophilic/hydrophobic substitution pattern **93** and/or altering the polarity by attaching non-polar part on one side of the porphyrin molecule, while attaching to the [hydrophobic] a polar part **94** (Figure 2.2).

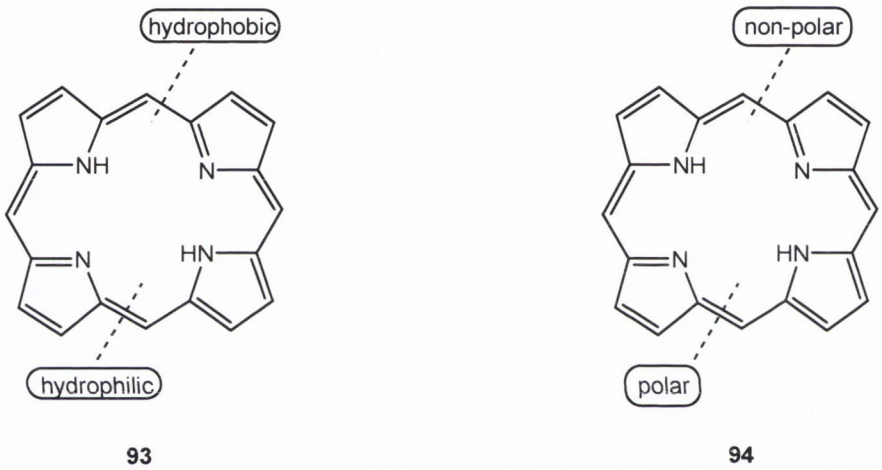


Figure 2.2. Schematic illustration of the basic structure of porphyrins suitable for PDT.

There are two possibilities to obtain such systems. The first possibility is to modify the ubiquitous occurring natural tetrapyrroles (chlorophylls and heme); the other possibility is the complete *de novo* synthesis of appropriate tetrapyrrolic systems. Verteporfin is an example of a PDT reagent synthesized using the first approach. The latter approach is exemplified by Temoporfin **92** [5,10,15,20-tetrakis(3-hydroxyphenyl)chlorin. Additionally, from an industrial perspective the syntheses of PDT reagents should be simple, facile and involve only a few synthetic steps. Hence, in order to synthesize lead structures as new photosensitizers, the synthetic methodology used should be simple and versatile to allow the preparation of series of compounds with minimal changes in the reaction conditions.

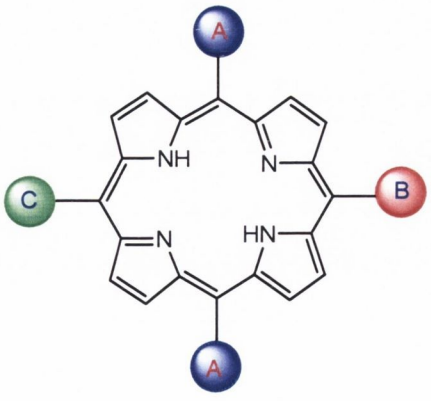
The *de novo* synthesis of unsymmetrically substituted (amphiphilic) tetrapyrroles may be achieved by a mixed condensation of pyrroles or dipyrromethanes with different aldehydes. Obviously, in the synthesis of highly unsymmetric porphyrins, such as A_2BC-type porphyrins,

complications that arise from this method are the number of potential regioisomers are very large. Subsequent purification and chromatographic workup is cumbersome.

Therefore, the ideal approach is the combination of these classical condensation reactions with subsequent functionalization by introducing different substituents directly at the free meso-positions *via* organometallic reagents or other C—C coupling reactions. In this chapter, we study how this combination of synthetic methods can be used to obtain, in a straightforward way, amphiphilic tetrapyrroles with a mixture of polar and nonpolar residues suitable for photodynamic therapy (PDT). Although our present study focuses on tetrapyrroles for amphiphilicity studies in PDT, this combination of methods is also suitable for the synthesis of unsymmetrically substituted porphyrins for other application areas, for example water-soluble porphyrins, multiporphyrin arrays, and optical applications (push-pull porphyrins for nonlinear optics).

2.2 Results and discussion

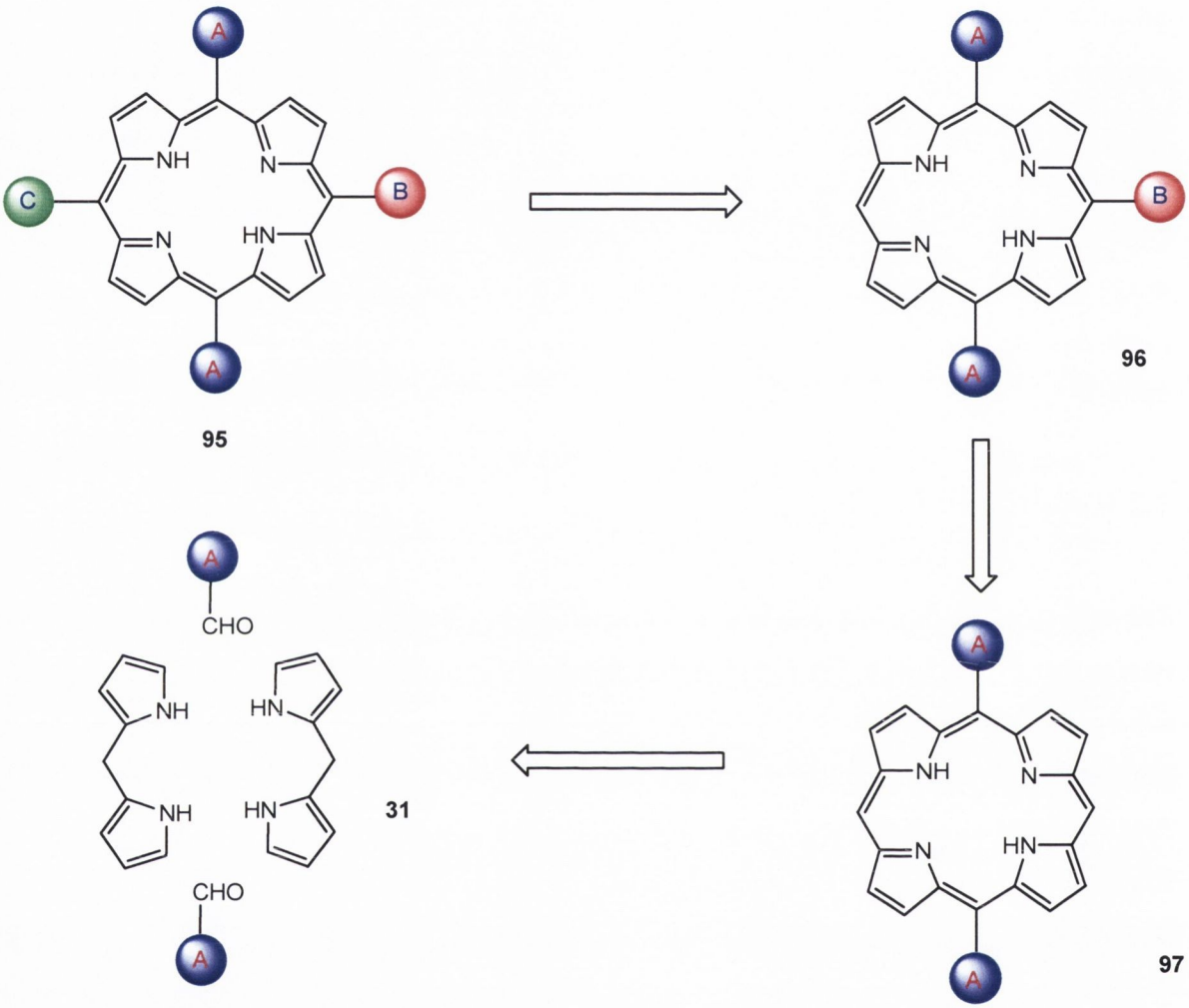
The aim of our study is to develop an efficient and versatile method to synthesize not only unsymmetric porphyrins but with substituents at the meso-positions that are suitable for subsequent transformations.[62] The synthetic methods used in this chapter are directed preferentially to a modification of easily accessible symmetric porphyrins. Thus, functionalized unsymmetric porphyrins A_2BC-type **95** (A = aromatic groups; B and/or C are substituents bearing functional groups) are the target compounds in this project and key intermediates for subsequent transformations (Figure 2.3).



95

Figure 2.3. Highly functionalized tetra-(A_2BC-type) meso-substituted unsymmetric porphyrin as a target compound.

The basic retrosynthetic approach for various functionalized tetra-(A_2BC-type) meso-substituted unsymmetric porphyrins **95** is illustrated in Scheme 2.1.

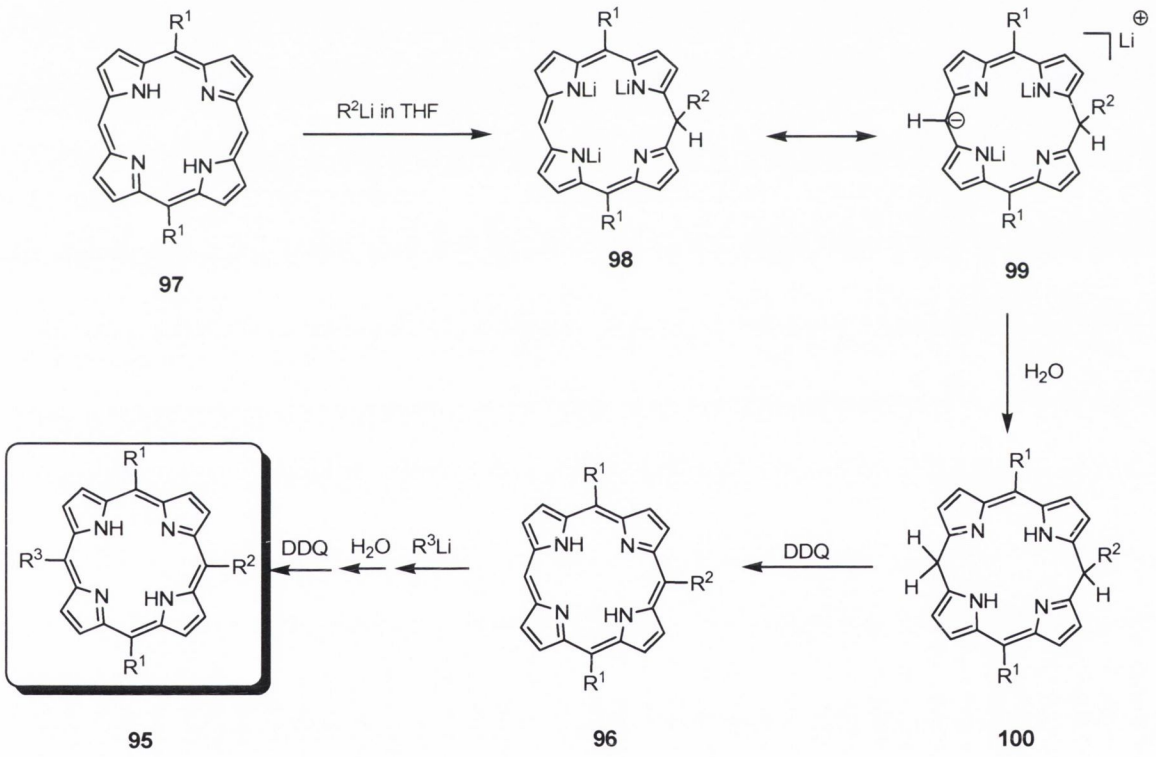


Scheme 2.1. Retrosynthetic analysis of A_2BC-type porphyrins.

It is shown that the synthesis of A_2BC free base porphyrins may start with the respective A_2-type free base porphyrins **97** which are easily accessible *via* a [2 + 2] condensation reaction using dipyrromethane **31** and an appropriate aldehyde.[48] Therefore, A_2B free base porphyrins **96** can be prepared *via* reaction of meso-disubstituted porphyrin (A_2-type) with an appropriate organolithium reagent introducing the "B" group.[62] Alternatively, possibilities exist to achieve this using Pd-catalysed coupling reactions. Further reaction of another appropriate

organolithium reagent with meso trisubstituted porphyrins (A_2B) **96** introducing the "C" group affords then the desired A_2BC porphyrins **95**.

The overall reaction of organolithium reagent with porphyrins is a nucleophilic substitution like the Ziegler alkylation[102], and proceeds *via* initial reaction of the organic nucleophile RLi with the free meso carbon in A_2-type free base porphyrins **97** yielding the phlorin-type intermediate **98** which converted to an anionic species **99**. Hydrolysis of **99** with water gives a 10,20-dihydroporphyrin **100**. Subsequent oxidation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) yields to the tri- (A_2B-type) meso-substituted porphyrin **96**. Repetition of the addition-oxidation sequence of R^3Li, H_2O and DDQ allows then the synthesis of unsymmetrically substituted (A_2BC) porphyrins **95** (Scheme 2.2).



Scheme 2.2. The general mechanism for the nucleophilic substitution reaction of free base porphyrins using organolithium reagents.

2.2.1 Synthesis of various highly functionalized amphiphilic A_2BC-porphyrins

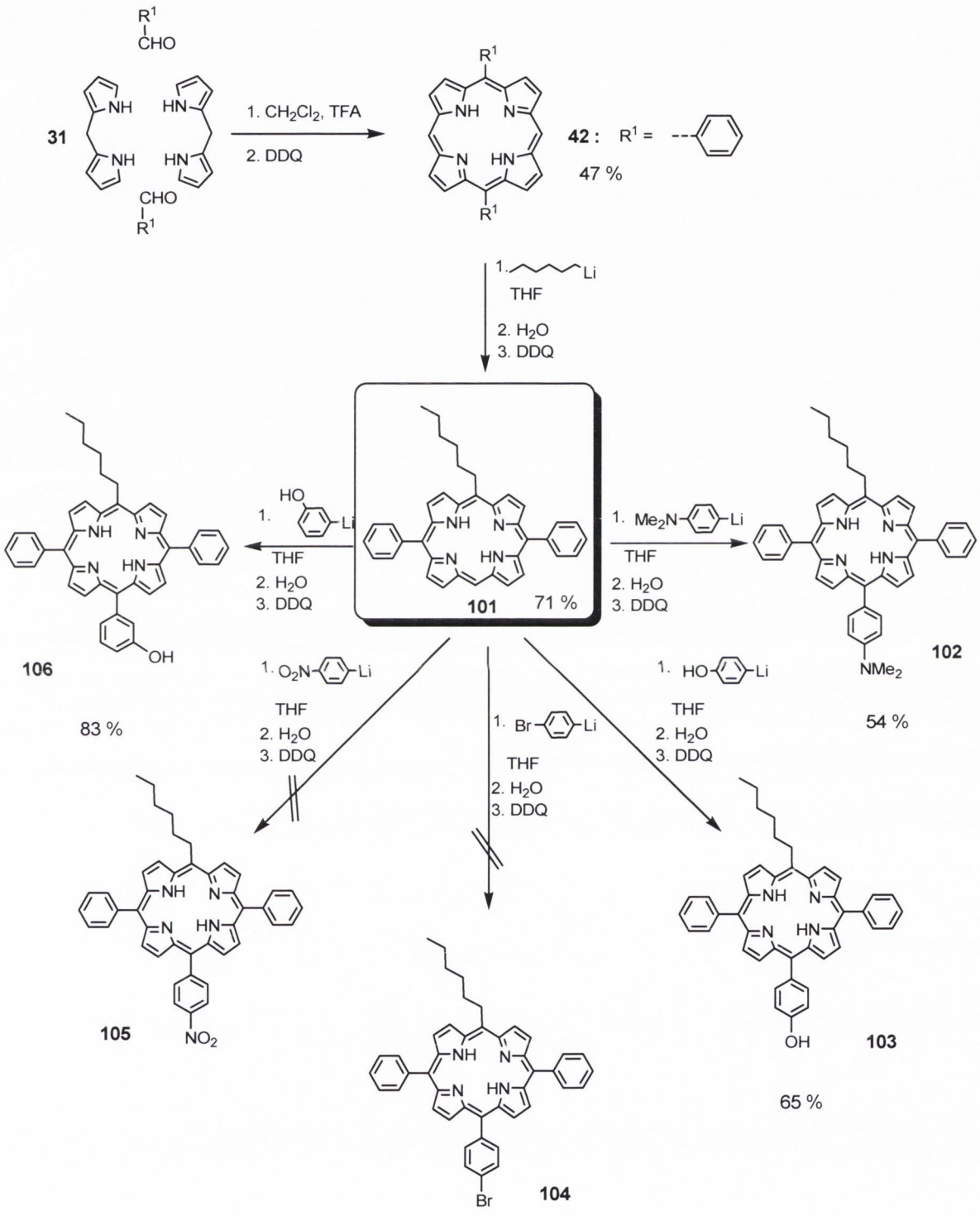
The symmetric porphyrin 5,15-diphenylporphyrin [H_2(DPP)] with two free meso-positions **42** (Scheme 2.3) was synthesized *via* [2 + 2] condensation reaction using dipyrromethane **31** and

benzaldehyde.[48] In order to introduce a non-polar group first to one of the two free meso-positions of **42**, the reaction of **42** with *n*-hexyllithium was employed to allow the synthesis of 5-hexyl-10,20-diphenylporphyrin **101** in 71 % yield. The functionalized porphyrins **102**, **103** and **106** were synthesized (Scheme 2.3) through the reaction of the *in situ* prepared corresponding functionalized organolithium reagents in excellent yields (60 — 80 %). The high yields achieved in this synthesis required more equivalents (10 — 15) of organolithium reagents which led to a higher concentration of LiOH in the reaction mixture after hydrolysis with water, therefore more DDQ (10-15 equivalents to porphyrins) was required as it is unstable in basic medium.[58,61,63,103] The excess of hydrolyzed organolithium reagents can be removed either through high vacuum distillation or by elution using an excess of *n*-hexane *via* chromatographic separation.[62]

The functionalized (A_2BC) porphyrins formed are much more polar than 5,15-diphenylporphyrin **42** and 5-hexyl-10,20-diphenylporphyrin **101** (especially for porphyrins bearing hydroxyl groups) and this allowed more easily chromatographic separation from each other. The functional groups introduced in Scheme 2.3 are reactive and easily employed in further reactions. For example, it is known from the literature that *p*-hydroxyl groups like those in porphyrin **103** react as nucleophiles smoothly with acid chlorides, anhydrides as well as with many halogen compounds.[104,105] Additionally, compound **103** may be considered as a key intermediate for many transformations to multiporphyrin arrays as the *p*-hydroxyl group in **103** can be coupled with various haloporphyrins to form porphyrin arrays with ether linkages.[106-109] Porphyrin **106** with a *m*-hydroxyphenyl substituent at the 15-position was synthesized in the highest yield (83 %).

Porphyrin **102** is a good intermediate for the synthesis of cationic derivatives by treatment with iodomethane. Such class of compounds is used as an entry into water-soluble cationic sensitizers for use in photodynamic therapy and is widely used for examinations of their interaction with proteins and DNA.[110] However, some aryllithium reagents with other functional groups could not be employed in this synthesis. Attempts to synthesize porphyrins bearing electron-withdrawing groups (such as -Br and $-NO_2$) **104** and **105** recovered only starting materials, indicating that *p*-bromophenyllithium and *p*-nitrophenyllithium reagents are not reactive towards 5-hexyl-10,20-diphenylporphyrin (Scheme 2.3).

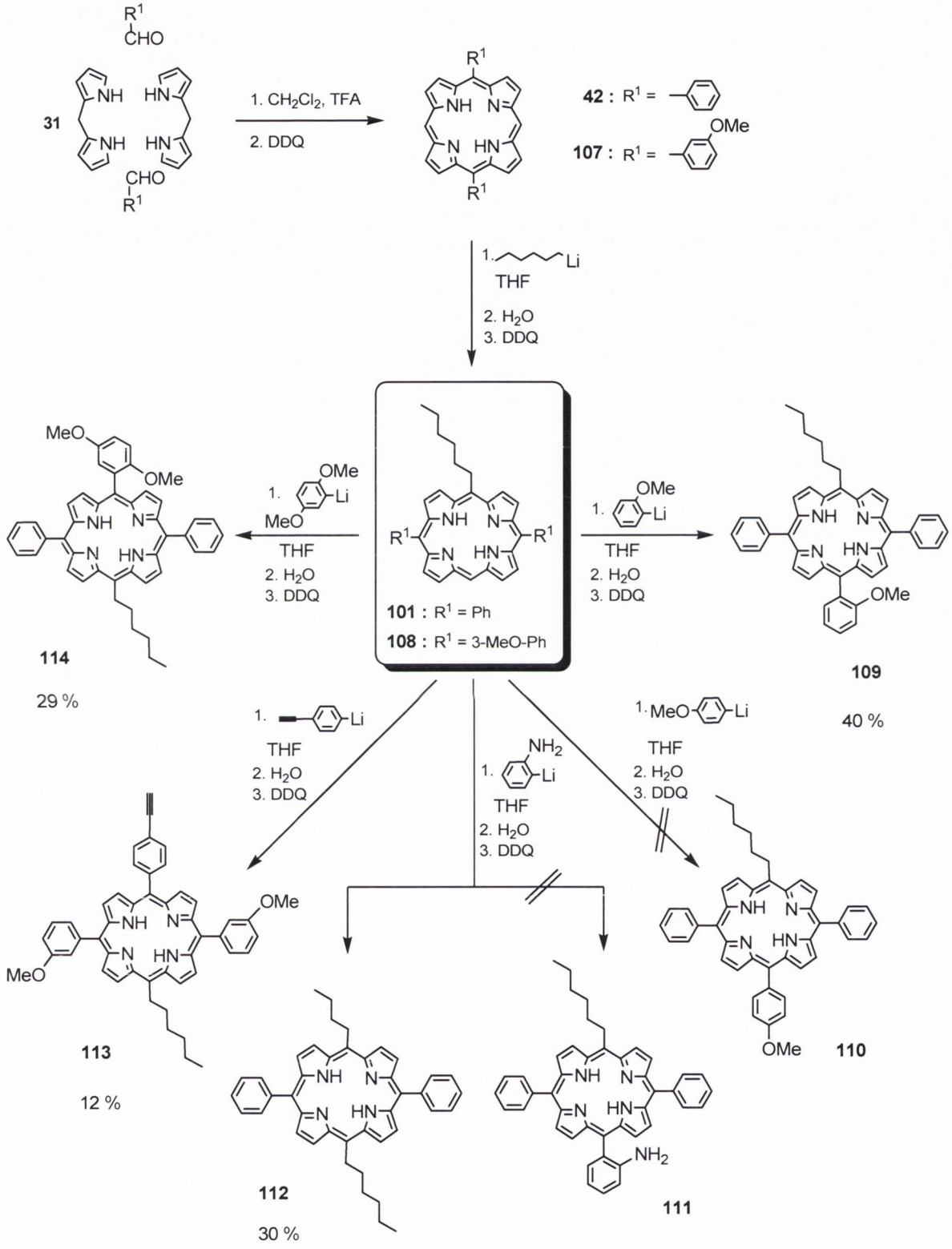
The study was then extended to the use of functionalized A_2-type symmetric porphyrins as a starting material such as 5,15-bis(3-methoxyphenyl)porphyrin **107**.



Scheme 2.3. Synthesis of A_2BC-type porphyrins using H_2(DPP) via S_NAr reactions.

In addition, different functionalized (A_2BC-type) unsymmetrical porphyrins (with methoxy, dimethoxy, or ethynyl groups) were synthesized successfully (Scheme 2.4). Using the same sequence as shown in Scheme 2.3, [2 + 2] condensation reactions with dipyrromethane **31** and benzaldehyde or 3-methoxybenzaldehyde can be used for the synthesis of DPP **42** and 5,15-bis(3-methoxyphenyl)porphyrin **107** followed by introducing non-polar group first to one of the two free meso-positions of **42** and **107** to yield **101** and **108**.The related functionalized porphyrins **109**, **113** and **114** were synthesized through the reaction of the corresponding functionalized organolithium reagents in moderate yields (20-40 %) (Scheme 2.4).

When the hydroxyl functional groups are protected, e.g., by using *o*-methoxyphenyllithium and 2,5-dimethoxyphenyllithium as reagents, the corresponding porphyrins **109** and **114** were successfully formed in yields of 40 and 29 % respectively. However, *p*-methoxyphenyllithium reagents showed surprisingly no reactivity with 5-hexyl-10,20-diphenylporphyrin **101** and the expected porphyrin **110** could not be isolated; only starting material was recovered. Surprisingly, in an attempt to synthesize the functionalized porphyrin **111** with *o*-aminophenyl substituent, porphyrin **112** was separated as the main product. This is believed to result from the attack of *n*-butyllithium to **101** to form porphyrin **112** in preference to the attack at *o*-aminophenyllithium reagent which was supposed to be performed *via* exchange reaction between *o*-aminophenylbromide and *n*-butyllithium. This could be due to the possible instability of the *in situ* prepared *o*-aminophenyllithium reagent and shifting the position of equilibrium to *n*-butyllithium and the bromide (Scheme 2.4).

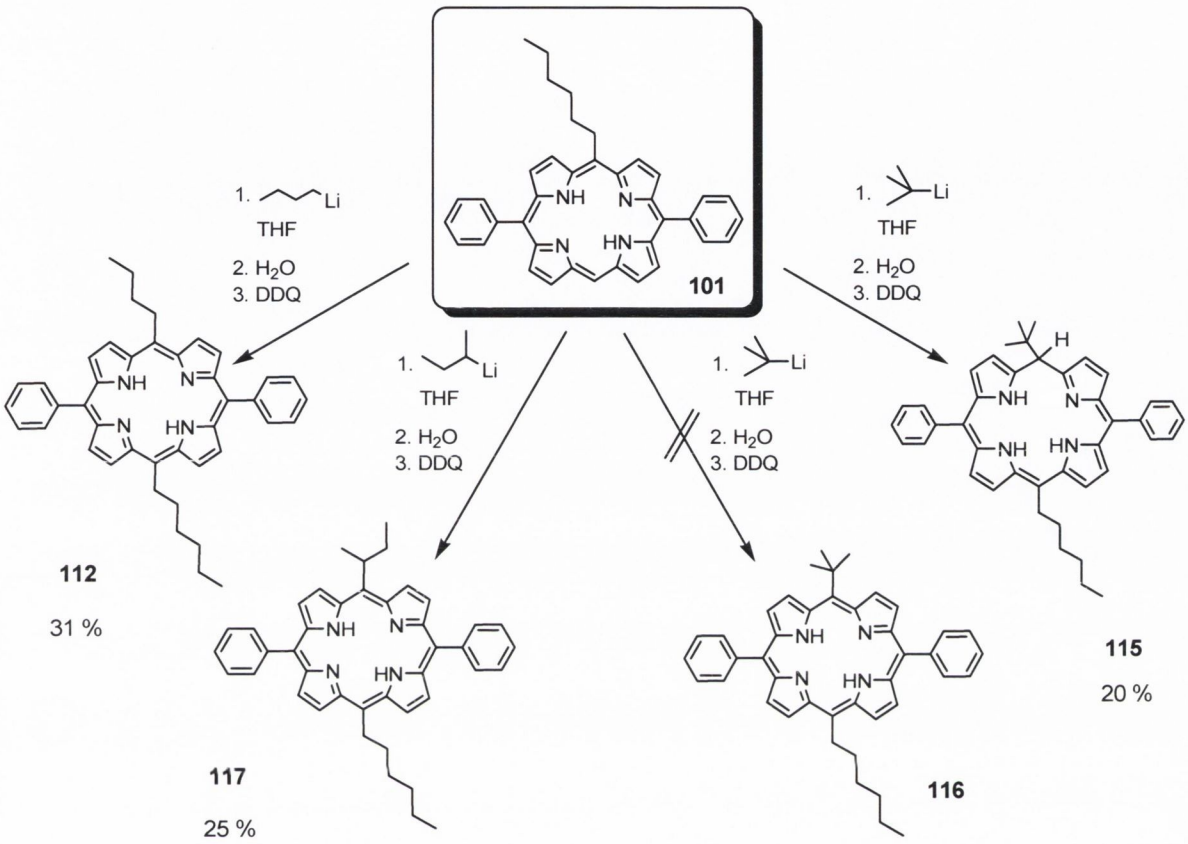


Scheme 2.4. Synthesis of different A_2BC-type porphyrins.

Here, the 5-(*p*-ethynylphenyl)-15-hexyl-10,20-bis(3-methoxyphenyl)porphyrin **113** formed, bearing a *p*-ethynyl group, and similar compounds have potential uses. They have found broad applications in the synthesis of superstructured materials, porphyrin arrays and porphyrin based materials such as push-pull porphyrins *via* Glaser or Heck coupling.[111-113] Couplings involving these compounds and *trans*-diiodides should give new unsymmetrical, linear trisubstituted porphyrins which may be used as model compounds for investigations of larger array systems. Generally, the potential of the porphyrin assemblies or arrays with alkyne bonds like in **113** has been investigated by Lindsey research group as light harvesters and molecular devices.[44,114,115]

This study was then extended to the utilization of meso-trisubstituted porphyrin **101** to carry different alkyl residues in the "C" position using butyllithium reagents with an increasing degree in steric demand. Reactions of *n*-, *sec*-, and *t*-butyllithium reagents with **101** were utilized to study the scope of their reactivity towards the meso-position under the same reaction conditions. Indeed, this approach was not only inspired by our aim to synthesize unsymmetrical A_2BC-type porphyrins but also by the known unusual behavior of *t*-butyl groups as sterically hindered reagents.[116] As shown in Scheme 2.5, *n*- and *sec*-butyllithium react in the same way with **101** to form the unsymmetrical porphyrins **112** and **117** in yields of 31 and 25 %, respectively. Interestingly, the reaction of *t*-butyllithium with **101** under the same conditions as with *n*- and *sec*-butyllithium preceeded in a different manner although the attack still directed to the more reactive meso-position. Thus, phlorin **115** was formed in 20 % yield instead of porphyrin **116**.[116] The NMR data are typical for a nonaromatic conjugated system with pyrrolic signals in the $\delta = 6 - 7$ ppm range. Mass spectra did not give the molecular ion peak for **115** (and for **122** in Scheme 2.8) and this is in regard to the other characterization techniques employed. The formation of phlorin **115** indicates that the free meso-position in **101** is more reactive towards *t*-butyllithium reagents than β-positions as no chlorin was separated in this case. These results are in line with results described by Callot and co-workers.[116]

The reaction sequence shown in Scheme 2.6 involved addition of *t*-butyllithium reagent to the porphyrin **101** to form **118**. The reaction was quenched with water to obtain phlorin **115** as the main product, which was isolated after oxidation with DDQ. This indicates the stability of phlorin **115** against oxidants. Indeed, this reaction opens a route for the conversion of free base porphyrins with free meso-position to phlorins with a variety of different meso-substituents. Formally, this constitutes an addition reaction involving two meso-positions.

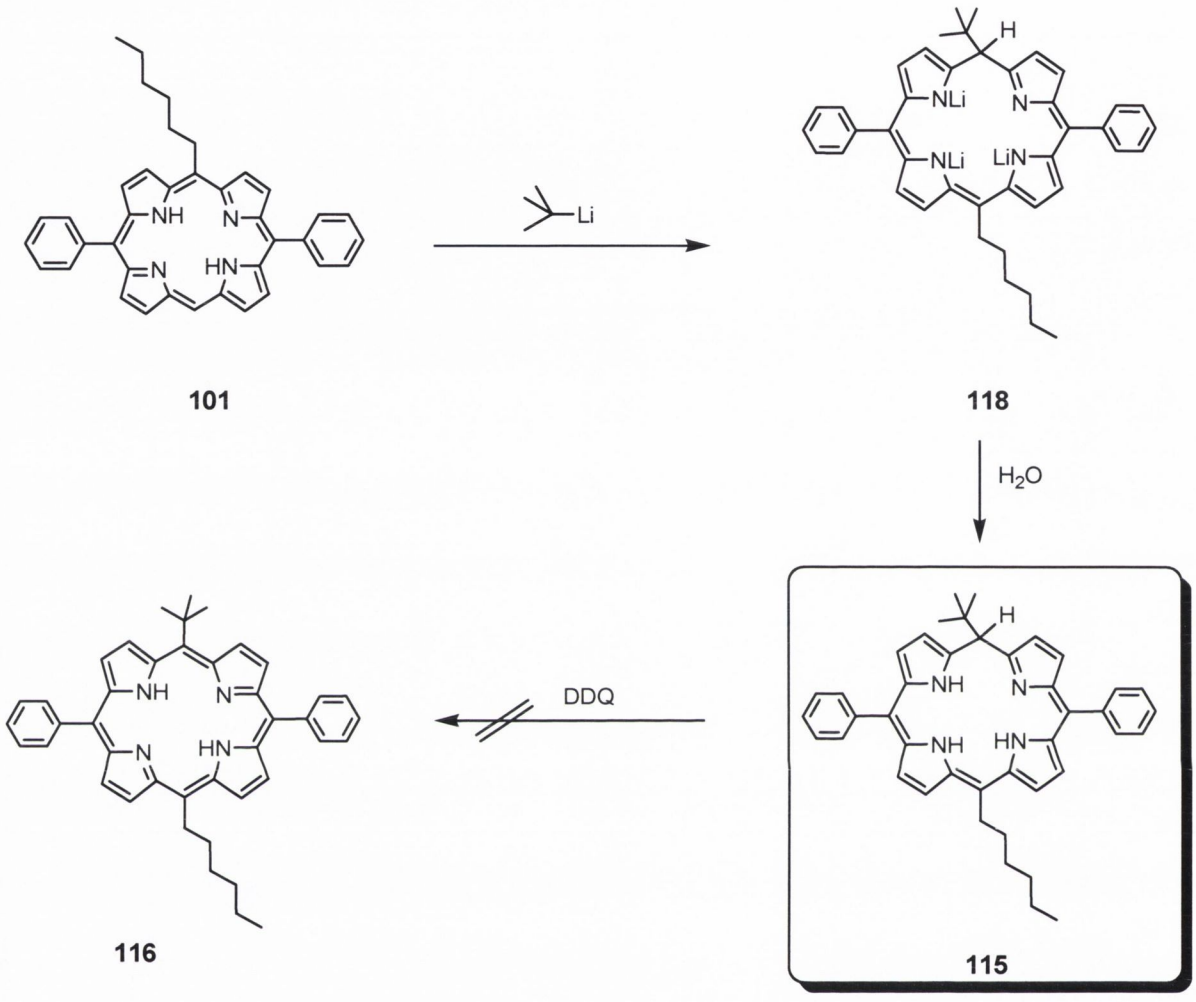


Scheme 2.5. Synthesis of A_2BC-type porphyrins and a phlorin using *n*-, *sec*-, and *t*-butyllithium reagents.

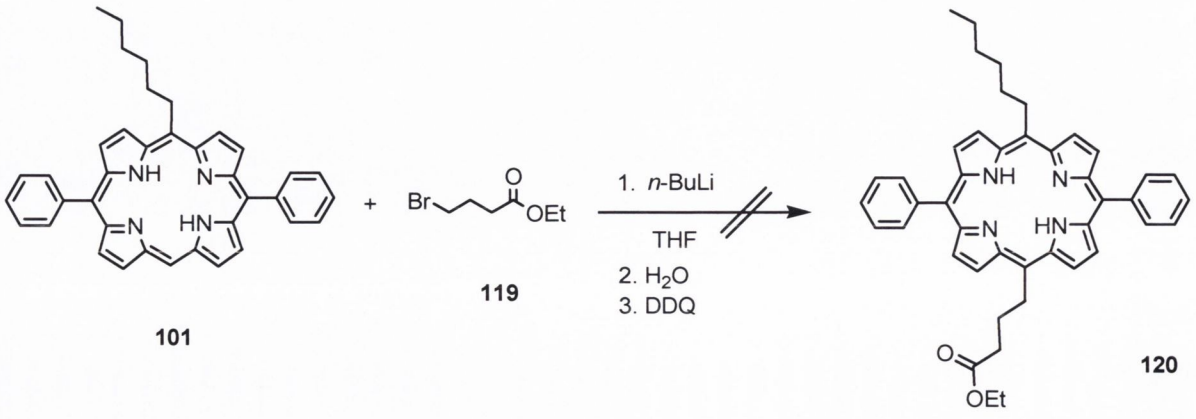
In addition, synthesis of an unsymmetric porphyrin containing an ester group was attempted through reaction of **101** with the *in situ* prepared lithiated ester of ethyl-4-bromobutyrate **119** *via* *n*-butyllithium reagent. Unfortunately, porphyrin **120** was not formed under the reaction conditions illustrated in Scheme 2.7.

The second part of the overall approach involved introducing different aryl and functionalized aryl groups instead of alkyl groups into the "B" position of the symmetric A_2-type porphyrins using organolithium reagents, followed by introduction of another substituent into the remaining "C" position. In general, introducing a variety of different aryl substituents into the "B" position to afford A_2B-type porphyrins was ideal and gave excellent yields (Scheme 2.8 and 2.9). However, attacking a meso-position opposite to one carrying an aryl group generally was difficult due to steric hindrance of the mesomeric benzylic anion stabilization.[58] Despite this, the synthesis of some A_2BC-type porphyrins by this method was successful. However,

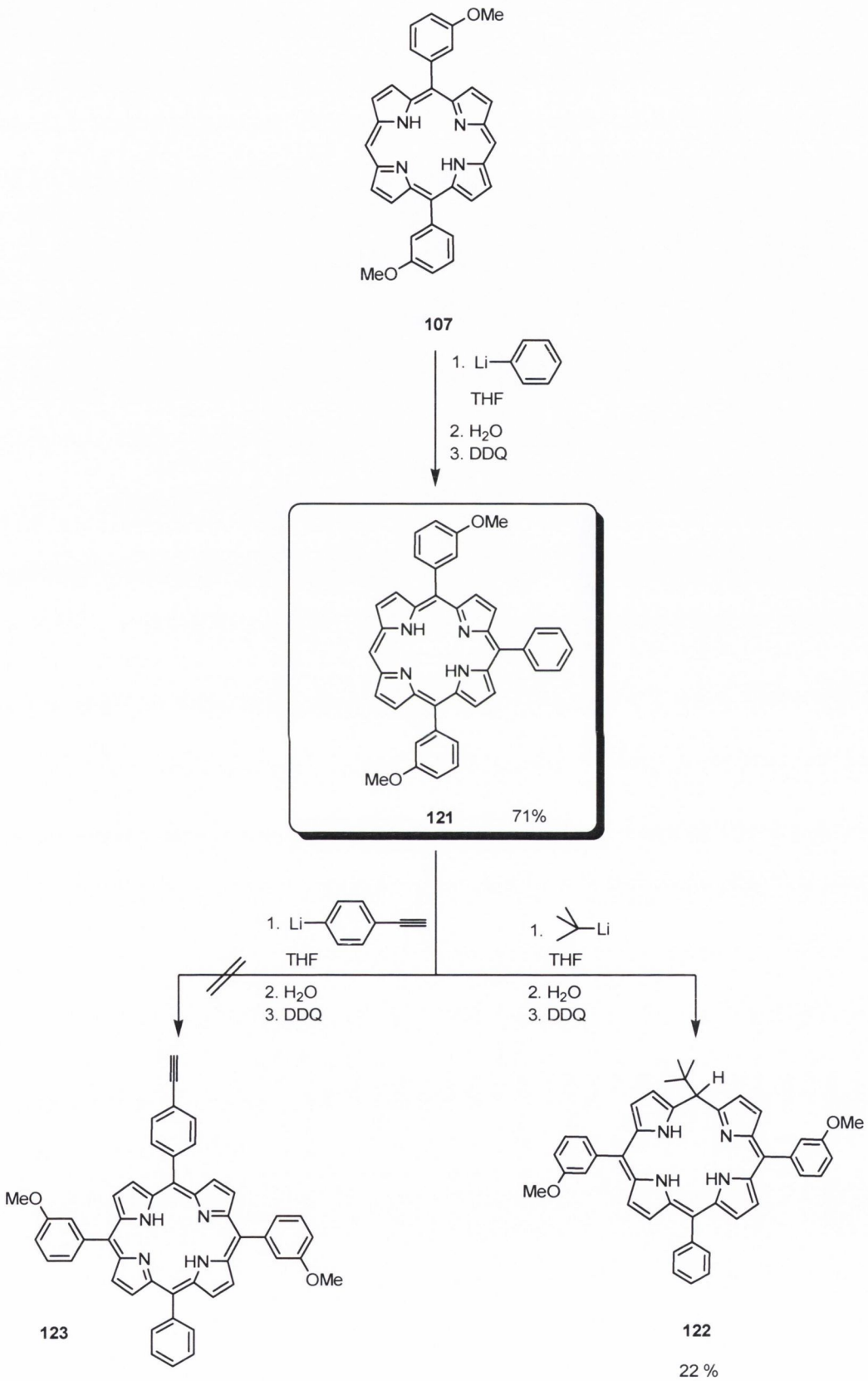
the yields obtained of these A_2BC-porphyrins were lower than those of A_2BC-porphyrins formed when B was an alkyl group.



Scheme 2.6. Mechanism of the addition of *t*-butyllithium to porphyrin **101**.



Scheme 2.7. unsuccessful reaction of **101** with ethyl4-bromobutyrate and *n*-butyllithium.



Scheme 2.8. Reactions of porphyrin **121**.

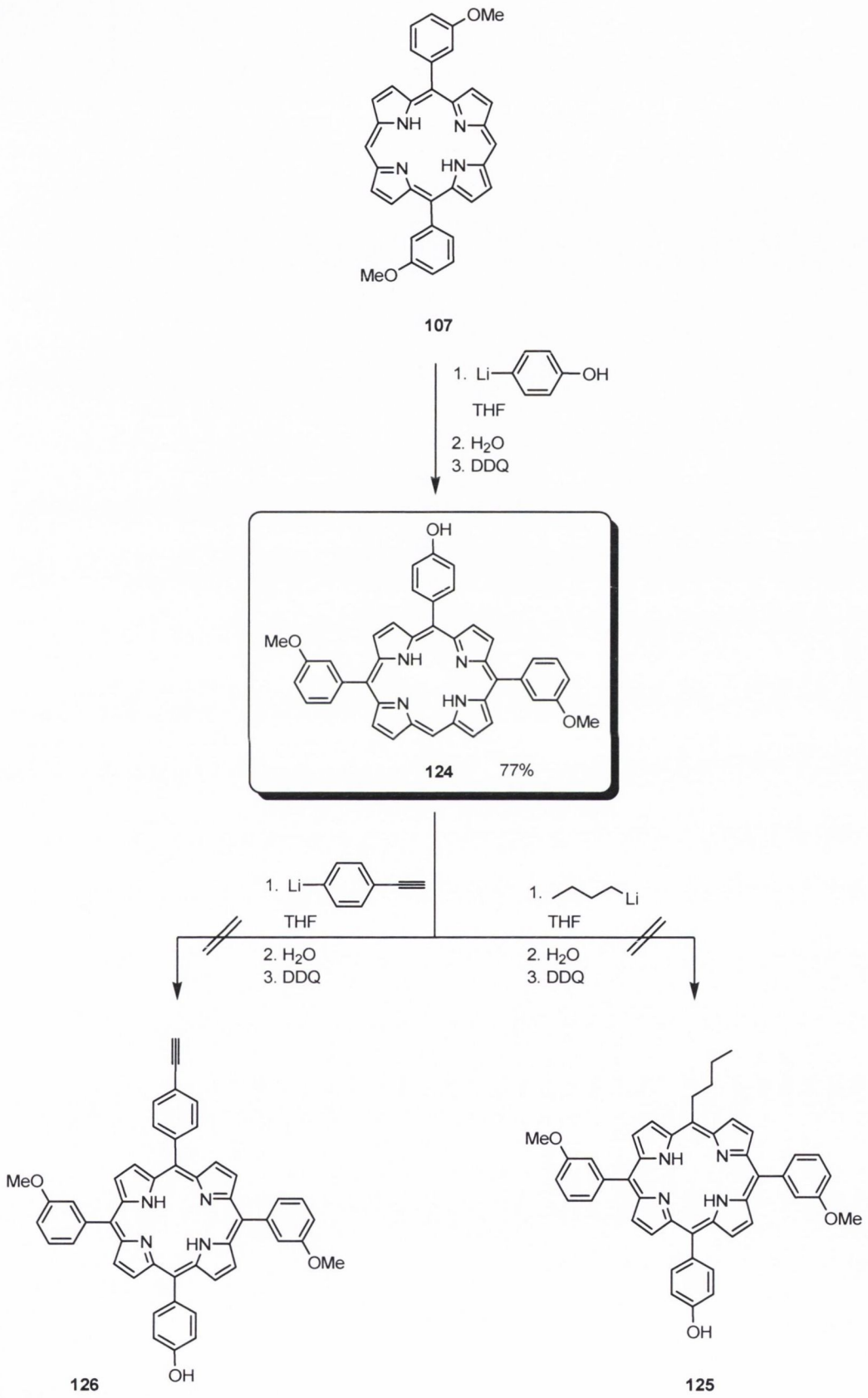
Initially, 5-phenyl-10,20-bis(3-methoxyphenyl)porphyrin **121** with an aryl substituent in the "B" position was synthesized in 71 % yield as a new A_2B-type porphyrin. *p*-Ethynylphenyllithium showed no reactivity towards **121** and the desired porphyrin **123** was not formed. However, *t*-butyllithium reacted with **121** to form the phlorin **122** in 22 % yield (Scheme 2.8). The mechanism for the formation of phlorin **122** is supposed to be the same as shown in Scheme 2.6.

Furthermore, functionalization of **107** using *p*-hydroxyphenyllithium was successful to afford 5-*p*-hydroxyphenyl-10,20-bis-(3-methoxyphenyl)porphyrin **124** as a new A_2B-type porphyrin in excellent yield of 77%. The reactivity of this compound was unsatisfactory. Neither *p*-ethynylphenyllithium nor *n*-butyllithium reacted with **124** under the standard conditions (Scheme 2.9).

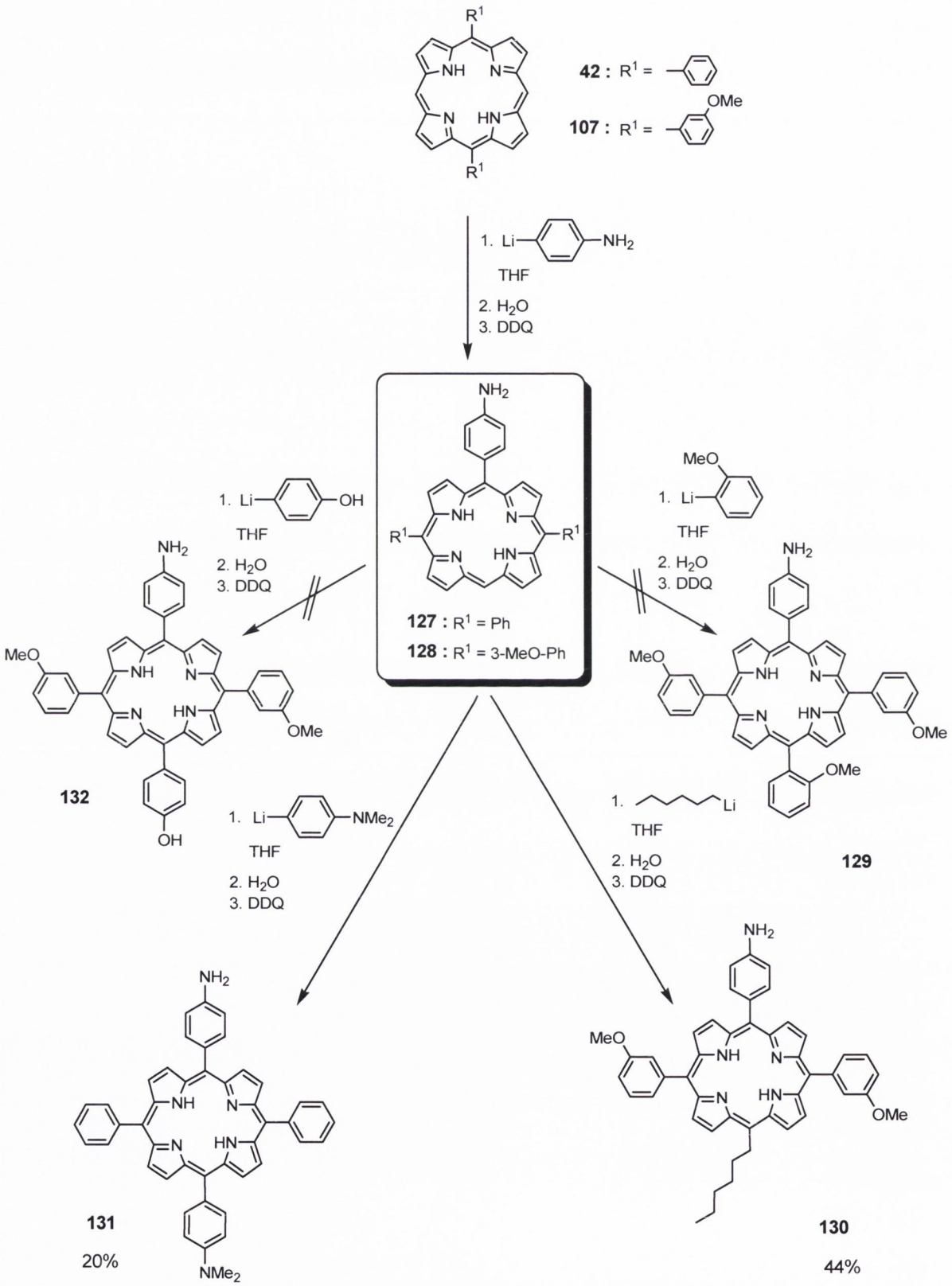
The final experiments for the meso-modification and functionalization were interesting. 5-(4-Aminophenyl)-10,20-diphenylporphyrin **127** and 5-(4-aminophenyl)-10,20-bis(3-methoxy-phenyl)-porphyrin **128** were successfully synthesized using 4-aminophenyllithium.[62] Although the *in situ* preparation of the 4-aminophenyllithium reagent from *n*-butyllithium and the corresponding bromide was done in high efficiency, it is particularly sensitive. Thus, it was very important to control all the factors during the reaction: (1) slow addition of *n*-butyllithium (ca. 1.5 — 2 h) at 0 °C; (2) stirring for another 1 — 1.5 h at R.T. until the solution became yellow-brown and a viscous material was observed at the bottom of the flask; (3) the cooled solution of the porphyrin was added to the vigorously stirred solution of RLi and not the other way around; (4) carring the experiments under very dry conditions, using argon atmosphere and dry THF.

Indeed, porphyrins with the *p*-aminophenyl group (strong electron donating group which make the porphyrin more electron rich) were targetted as a key intermediate for the synthesis of amphiphilic porphyrins, where further functional groups can be inserted into the free meso-position by another reaction with RLi. However, utilization of amino-functionalized meso-trisubstituted porphyrins **127** and **128** as starting materials gave mixed results (Scheme 2.10).

The porphyrin **130** with non-polar substituent (hexyl group) at the "C" position was synthesized through the reaction of *n*-hexyllithium with 5-(4-Aminophenyl)-10,20-bis(3-methoxyphenyl)-porphyrin **128** in 44 % yield and the porphyrin **131** was synthesized through reaction of *p*-dimethylaminophenyllithium with 5-(4-aminophenyl)-10,20-diphenylporphyrin **127** in 20 % yield. Unfortunately, the porphyrins **129** and **132** were not formed as the respective lithium reagents showed no reactivity against porphyrin **128** (Scheme 2.10).



Scheme 2.9. Reactions of porphyrin **124**.



Scheme 2.10. Porphyrins containing a *p*-aminophenyl group as key intermediates for further transformations.

2.2.2 ^{1}H-NMR spectroscopy of β-, meso and N—H protons of A_2-, A_2B- and A_2BC-porphyrins

The ^{1}H NMR spectroscopic pattern of the β-pyrrole hydrogens of substituted porphyrins depends on various factors. One of the important factors is the symmetry inherent in the porphyrin molecule. Consequently, the pattern of the β-pyrrole hydrogen ^{1}H NMR signals can be used to identify the symmetry of the porphyrin.[117] Other factors include the type, number and arrangement of various substituents in the meso positions.[59] By taking all these factors into consideration, we can analyze the spectra of A_2-, A_2B- and A_2BC-type porphyrins.

Generally, the ^{1}H signals of porphyrins depend on the distance and orientation of the protons with respect to the π electrons of the macrocyclic ring system with protons above or inside the ring being shielded and those outside the ring being deshielded.[118] Thus, the ^{1}H NMR signals of the characteristic groups can be easily distinguished as follow: (1) $\delta H_\beta = \sim 8 - 9.5$ ppm, (2) $\delta H_{meso} = \sim 10$ ppm, (3) $\delta N{-}H < 0$ ppm.

The successful preparation of unsymetrically substituted porphyrins with various substituent types allows a comparative analysis of the changes in the NMR spectra of β-hydrogen atom splitting and chemical shift. It is convenient to begin this comparison by looking at the completely unsubstituted porphyrin, porphine **1**, as a standard molecule and moving to A_2-, A_2B- and finally to A_2BC-porphyrins to observe the effect of different numbers and regiochemical arrangements of meso substituents and their effect on the symmetry of the molecules. The different positions and numbers of the symmetry axes of each is responsible for the different NMR patterns.[117,119,120] Porphine **1** has four symmetry axes, two of them passing through the meso carbons and the other two bisecting the pyrrole units. Thus, the β-pyrrole protons (H2/H3/H7/H8/H12/H13/H17/H18), being magnetically equivalent, give a singlet at 9.56 ppm and similarly the four meso protons (H5/H10/H15/H20) exhibit a singlet at 10.41 ppm (Figure 2.4). 5,15-Bis(*m*-methoxyphenyl)-porphyrin **107** (A_2-type) has two symmetry axis and consequently the pattern of the β-pyrrole protons shows two AB systems for the non-equivalent protons at 9.16 (H3/H7/H13/H17) and 9.43 ppm (H2/H8/H12/H18), respectively, and the two meso protons (H10/H20) exhibit a singlet at 10.35 ppm (Figure 2.5). 5-(4-Aminophenyl)-10,20-bis(3-methoxyphenyl)-porphyrin **128** is taken as an example for the A_2B-type systems. Porphyrin **128** has only one symmetry axis passing through the free meso position and the opposite 4-aminophenyl group (Figure 2.6).

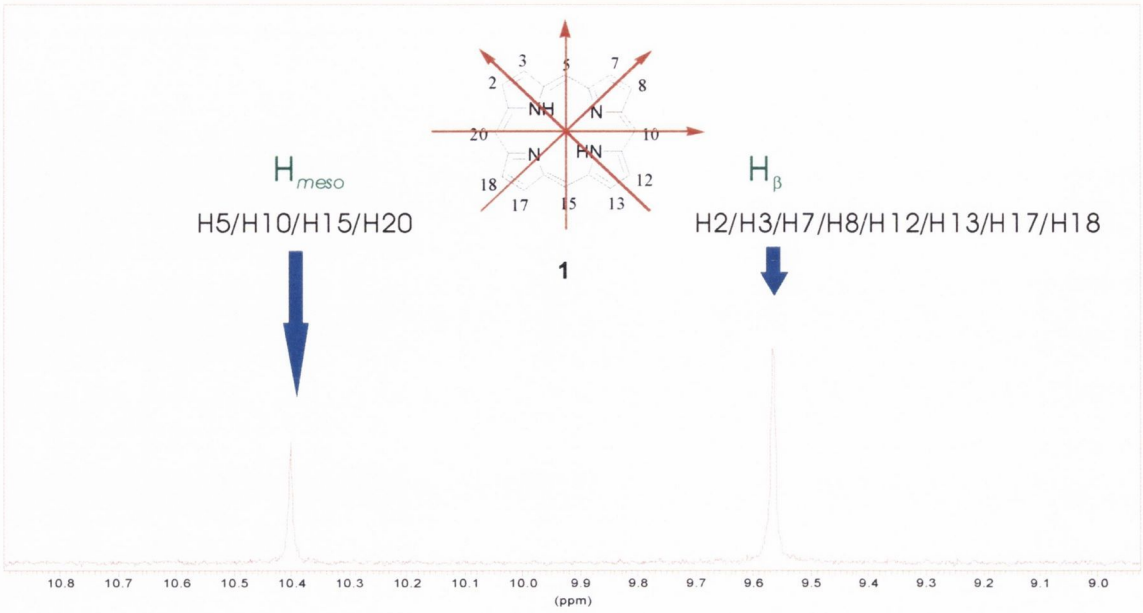


Figure 2.4. ^{1}H NMR spectraum of the β-pyrrole and meso hydrogens of **1** in $CDCl_3$.

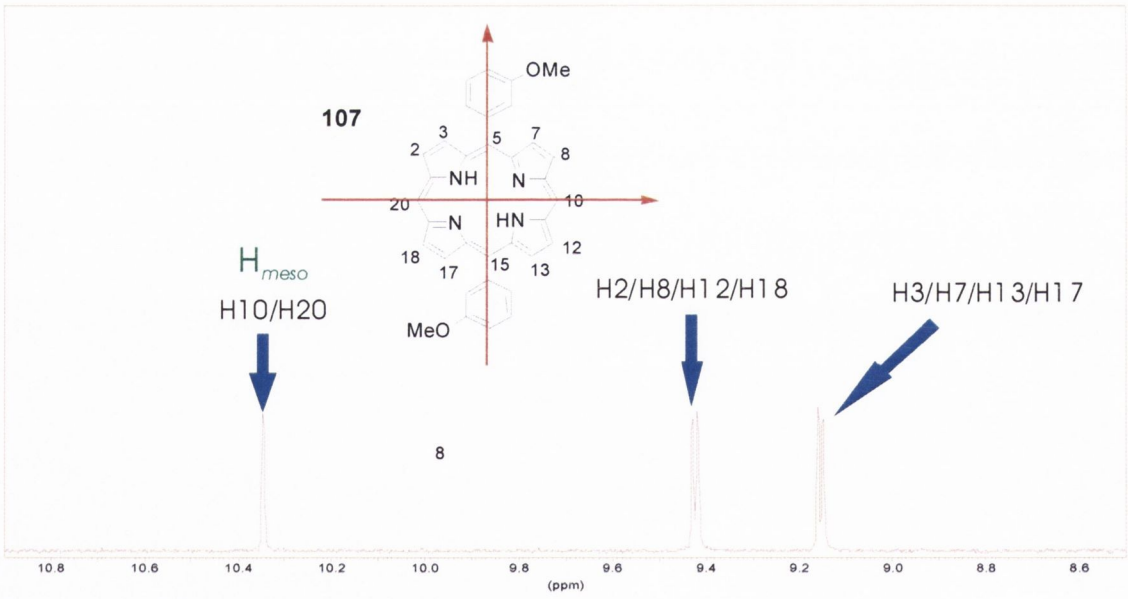


Figure 2.5. ^{1}H NMR spectrum of the β-pyrrole and meso hydrogens of **107** in $CDCl_3$.

Consequently, the pattern of the β-pyrrole protons shows three different sets of nuclei as two doublet close in the chemical shift for H2/H8/H12/H18 at 8.98 ppm and two AB signals at 9.05 and 9.35 ppm for H3/H7 and H13/H17, respectively, while the meso proton H15 give a singlet at 10.21 ppm (Figure 2.6). The upfield shift of the β-protons H3 and H7 with respect to

H13 and H17 by 0.3 ppm results from the ring-current effect of the adjacent phenyl ring in the case of H3 and H7 as they are located in this shielding region above and below the phenyl plane, since aryl substituents lie approximately orthogonal to the plane of the porphyrin.[59,121]

Finally, for our comparative analysis of the changes in the NMR spectra of β-pyrrole protons, two different unsymetrically substituted porphyrins (A_2BC-type) were examined. The first compound was 5-(*sec*-butyl)-10,20-diphenyl-15-hexylporphyrin **117** with B and C as meso-alkyl residues. Porphyrin **117** has only one symmetry axis passes through the *sec*-butyl group and the opposite hexyl group (Figure 2.7) and the pattern of the β-pyrrole protons shows three different set of nuclei as two doublets possessing similar chemical shifts for H2/H8/H12/H18 at 8.86 ppm and two doublets at 9.43 and 9.57 ppm (J = 5.0 Hz) for H13/H17 and H3/H7, respectively. As H2/H8/H12/H18 are in proximity to two phenyl groups, they undergo more upfield shifts than H13/H17 and H3/H7 (in proximity to aliphatic groups) due to the ring current effect of the two phenyl groups as mentioned previously (Figure 2.7).

5-(*p*-Ethynylphenyl)-15-hexyl-10,20-bis(*m*-methoxyphenyl)porphyrin **113** is the second example examined of A_2BC-type but with a meso-alkyl residue as B and a meso-aryl residue as C. Porphyrin **113** has also one symmetry axis passing through the *p*-ethynylphenyl group and the opposite hexyl group (Figure 2.8) and the pattern of the β-pyrrole protons was different in this case. Porphyrin **113** shows four different sets of two magnetically equivalent nuclei as doublets (H2/H8 at 8.78 ppm, H12/H18 at 8.88 ppm, H3/H7 at 8.98 ppm, H13/H17 at 9.51 ppm, respectively) (J = 5.0 Hz). As H13 and H17 are the only two protons not in proximity to an aryl group (closest to hexyl group), they appear as the ones with the most downfield shift compared to H3 and H7 (closest to *p*-ethynylphenyl group) or H2, H8, H12 and H18 (closest to *m*-methoxyphenyl group). The β-pyrrole protons H2/H8 exhibit a doublet at 8.78 ppm while H12/H18 show doublet at 8.88 ppm in porphyrin **113** rather than identical chemical shifts as in porphyrin **117** because H2/H8 are flanked by *p*-ethynylphenyl and *m*-methoxyphenyl groups while H12/H18 are flanked by hexyl and *m*-methoxyphenyl groups (Figure 2.8).

The porphyrin N–H protons appear at 0 to − 4 ppm because of the strong upfield shift caused by the macrocycle ring current effect.[121] Depending on the degree of substitution, the N–H signals undergo low-field shifts with increasing number of meso-substituents.[59] Figures 2.9 illustrates the downfield shift of the N-H proton signals from porphine **1** (− 3.93 ppm) to porphyrin **107** (A_2) (− 3.12 ppm) to **128** (A_2B) (− 2.99 ppm) to **117** (A_2BC) (− 2.56).

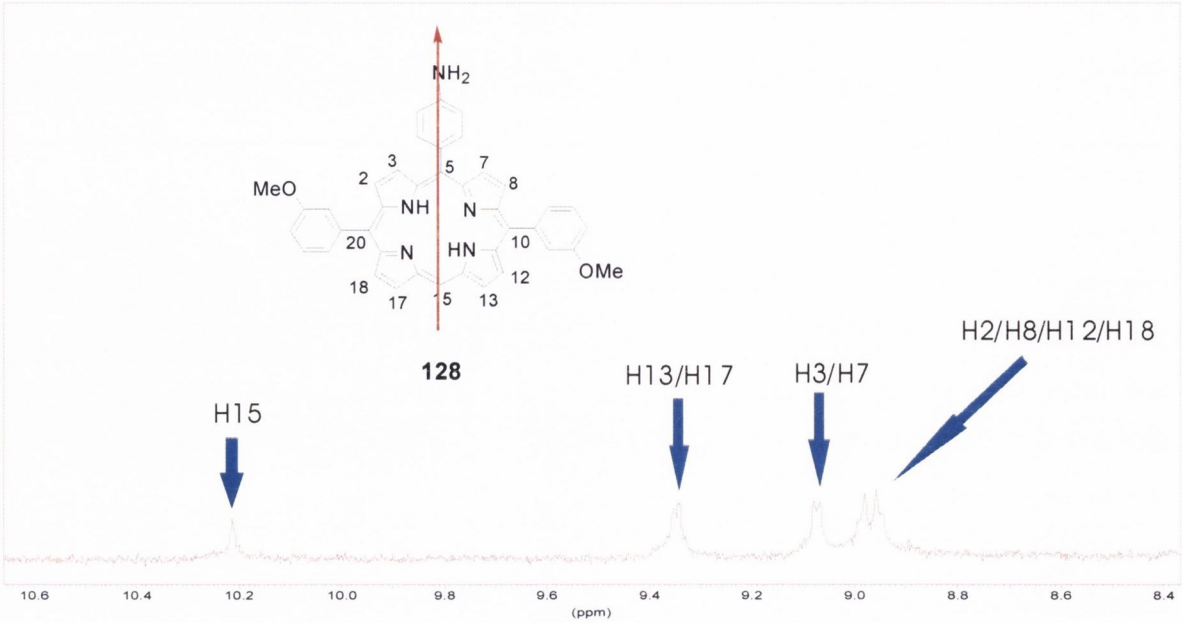


Figure 2.6. ^{1}H NMR spectrum of the β-pyrrole and meso hydrogens of **128** in $CDCl_3$.

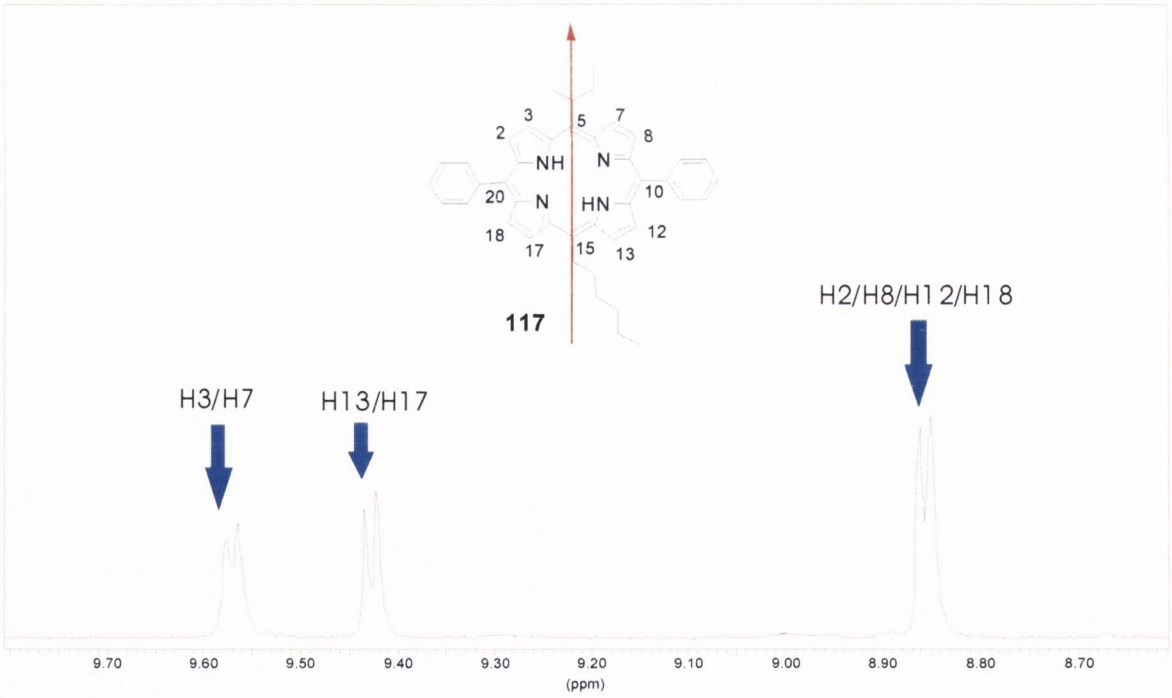


Figure 2.7. ^{1}H NMR spectrum of the β-pyrrole hydrogens of **117** in $CDCl_3$.

Similar spectral habits were found for various substituted porphyrin (not shown). Thus, the ^{1}H NMR spectra allow a clear identification of the number, arrangement and symmetry of aryl substituents in the series of meso-substituted porphyrins.[117,119,120]

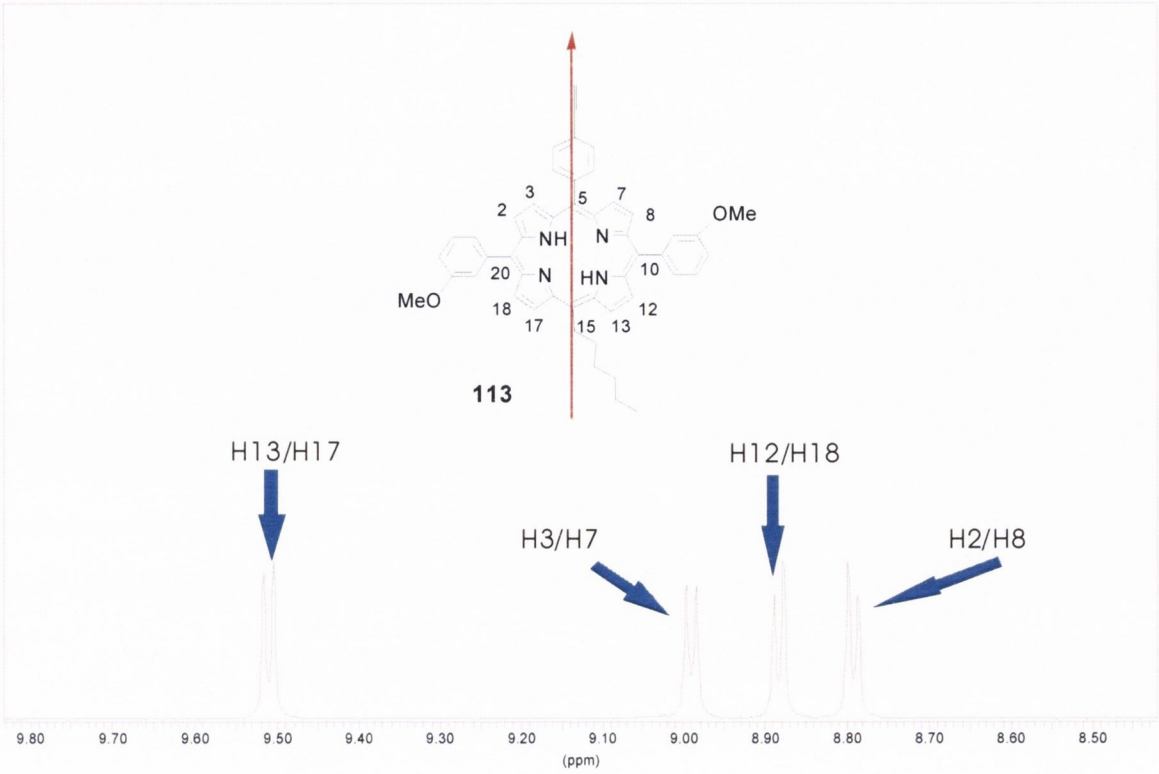


Figure 2.8. ^{1}H NMR spectrum of the β-pyrrole hydrogens of **113** in $CDCl_3$.

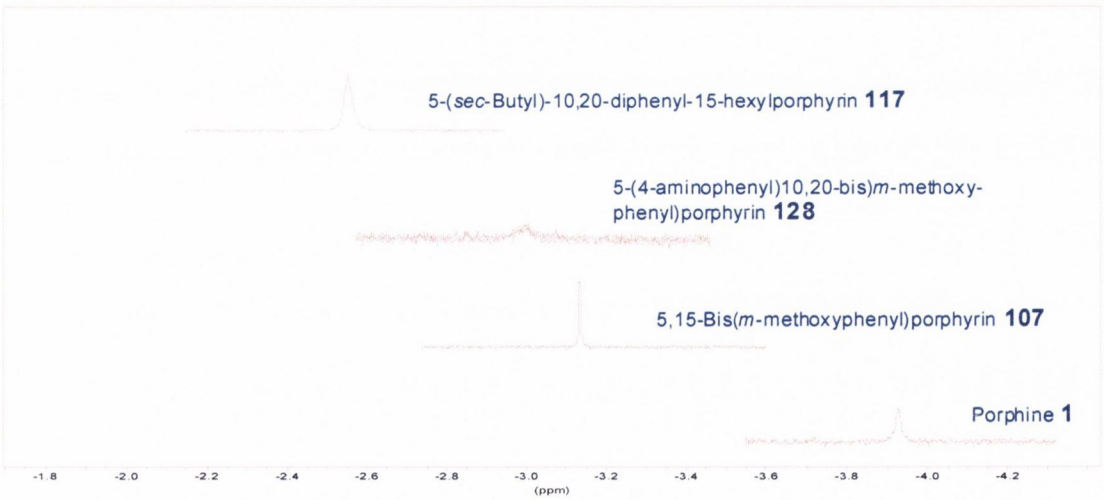


Figure 2.9. ^{1}H NMR spectrum of the N–H hydrogens of porphyrins **1**, **107**, **128** and **117** in $CDCl_3$.

2.3 Conclusions

Starting from the medicinal applied science oriented approach we have shown how the present tools of synthetic porphyrin chemistry could be combined together to obtain a wide variety of unsymmetrically substituted amphiphilic porphyrins as potential lead structures for use in photodynamic cancer therapy.

The symmetric porphyrin starting materials (A_2-porphyrins) were easily prepared by simple condensation reactions of dipyrromethane and suitable aldehydes. These porphyrins were then functionalized by a nucleophilic aromatic substitution reaction (S_NAr) with a wide variety of aliphatic and aromatic organolithium compounds, allowing the introduction of, for example alkyl chains, phenyl groups, free hydroxyphenyl groups, protected phenolic groups in different positions, aminophenyl substituents, dimethylaminophenyl substituents, or ethynylphenyl substituents.

A_2BC free base porphyrins could be prepared *via* reaction of meso-trisubstituted porphyrins (A_2B) with an appropriate organolithium reagent introducing the "C" groups. If A_2B porphyrin carries an alkyl residue in the "B" position, reaction with ArLi generally gave better yields than alkyl lithium reagents. On the other hand, attacking a meso-position opposite to one carrying an aryl group generally gave lower yields, due to steric hindrance of the mesomeric benzylic anion stabilization. Nevertheless, this method allowed the preparation of the target compounds with acceptable yields and in two steps from the respective A_2 porphyrins.

Finally, even though some limitations remain concerning some functional groups, this methodology could be useful from the synthetic point of view and opens a practical way to synthesize more highly functionalized substituted porphyrins with a mixed hydrophilic/hydrophobic substitution pattern which could be used towards applications in PDT.

Chapter 3

One-pot synthesis of A_2BC-type free base porphyrins

3.1 Introduction

Unsymmetric A_2BC-porphyrins whose meso substituents contain functional groups or chemically reactive groups, can present suitable precursors for transformations into amphiphilic porphyrins for medicinal applications (PDT) or for the synthesis of more complicated porphyrin systems like multiporphyrin assemblies for optical applications.[122-124] The increasing importance of these applications provides continual stimulus for intensive research towards artificial functionalized unsymmetric porphyrins. However, at present it is difficult to introduce multiple functional groups to the porphyrin moiety to form the target unsymmetric porphyrins.

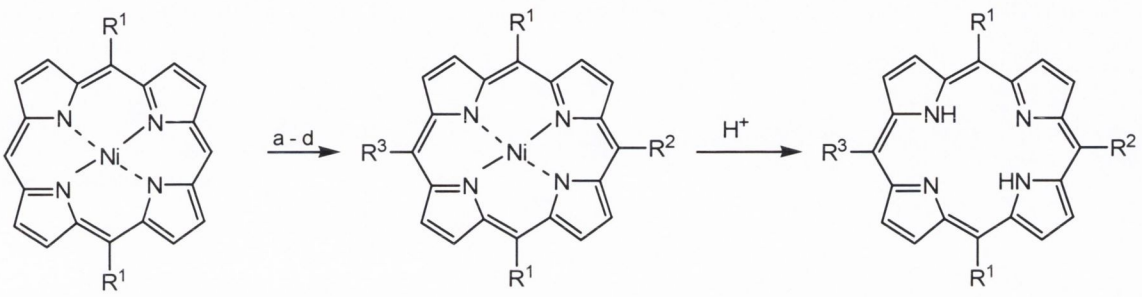
In general, there have been few synthetic methods to reach A_2BC-porphyrins. Nevertheless, three of the most common synthetic approaches to yield such compounds, the first one being multi-step total syntheses, while the second involves mixed condensations which require tedious chromatographic separation. The third approach is palladium-catalysed coupling and functionalization to the porphyrin macrocycle which is a topic of considerable interest in the recent literature.[44,65-67,112]

As mentioned previously, our research group have made considerable progress in this area *via* direct introduction of different functional groups *via* organolithium reagents. A reaction sequence of addition of RLi, hydrolysis with water, and subsequent oxidation with DDQ allowed the convenient and mostly quantitative preparation of porphyrins with different meso substituents. However, in some cases, the desired functional groups (with oxygen, nitrogen or halogen atoms) are not tolerated by organolithium reagents and react rapidly with them. Thus, such reactive groups must be protected at first and after that refunctionalized by another reagent. Therefore, the synthesis of unsymmetric (A_2BC) porphyrins *via* this method is limited to the introduction of one substituent in each reaction step.

Indeed, these limitations stimulated the search for a more facile synthetic method to obtain the target functionalized unsymmetric porphyrins *via* fewer synthetic steps.

As mentioned in Chapter 1 during more detailed mechanistic investigations of the reaction of RLi with (5,15-dialkyl/arylporphyrinato)nickel(II) **133,** Senge and Feng found that the addition of electrophilic reagents such as alkyl iodide "after the hydrolysis step," followed by oxidation with atmospheric oxygen, permits the preparation of functionalized unsymmetric tetrasubstituted porphyrins **134** which can be converted to the free base porphyrins **95** by using

very strong acids.[125] The use of an electrophile was inspired by the formation of reactive carbanion intermediates[56,64,126] (Meisenheimer-type[127] porphodimethene anions) entailed by the reaction mechanism. The *in situ* trapping of these intermediates with electrophiles; and the reaction can be considered as two-step one-pot reaction (Scheme 3.1).[63]



133 **134** **95**

Reagents and conditions: (a) R^2Li, THF, -70 °C; (b) H_2O; (c) R^3I, 1 h, RT; (d) oxidation (air or DDQ).

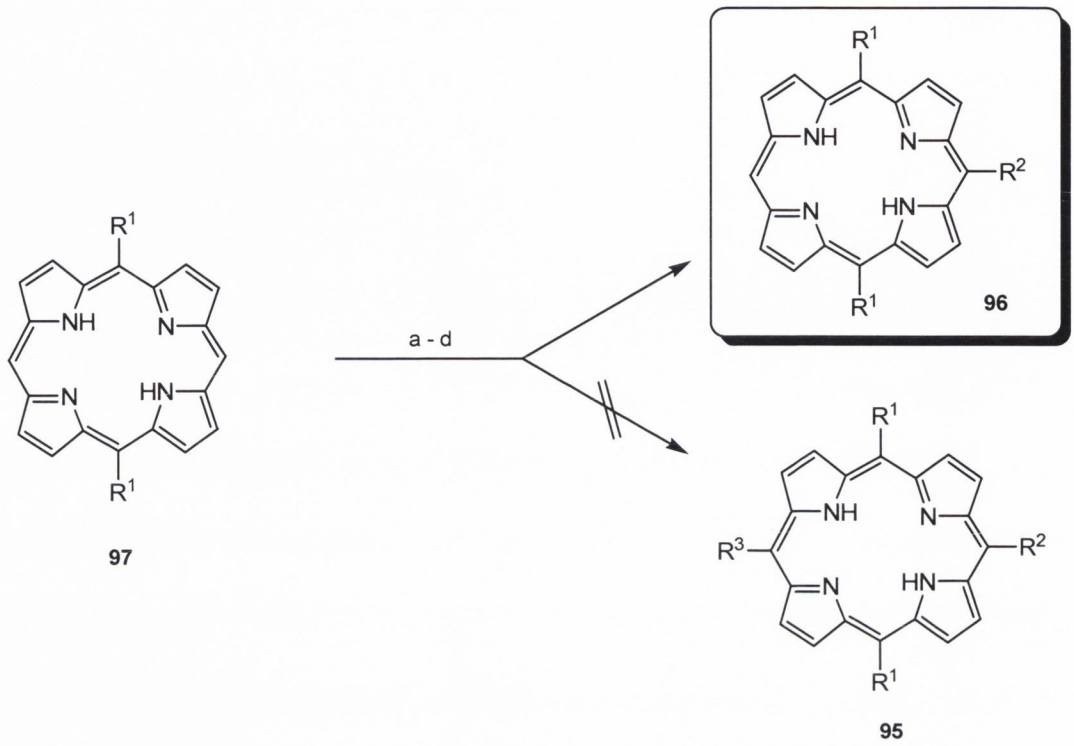
Scheme 3.1. Standard reaction of (5,15-A_2-porphyrinato)nickel(II) with R^2Li/R^3I.

On the other hand, they found that using the respective free base porphyrins **97** under similar reaction conditions gave 5,10,15-trisubstituted (A_2B-type) porphyrins **96** as the sole product without formation of A_2BC-type porphyrins **95**, similar to the standard reaction sequence (Porphyrin, RLi, H_2O and DDQ) without use of alkylyliodide (Scheme 3.2). In addition, mechanistic studies indicated a phlorin anion to be the key intermediate of this reaction.[56] Therefore, the synthesis of A_2BC-type free base porphyrins **95** *via* S_NAr reactions necessitated either two addition-oxidation sequences using two different LiR reagents or first preparation of **134** followed by demetalation; the latter typically requiring harsh reaction conditions (e.g., very strong acids or BBr_3).[125]

3.2 Results and discussion

The aim of our study was to develop an easy and versatile method to synthesize functionalized unsymmetrically substituted A_2BC-porphyrins with substituents at the meso positions (A_2BC-

type). To do this, a one-pot two-step disubstitution of free base 5,15-disubstituted A_2-type porphyrins was attempted.[48,125,128,129] In earlier work using 2,3,7,8,12,13,17,18-



Reagents and conditions: (a) R^2Li, THF, -70 °C; (b) H_2O; (c) R^3I, 1 h, RT; (d) oxidation (air or DDQ).

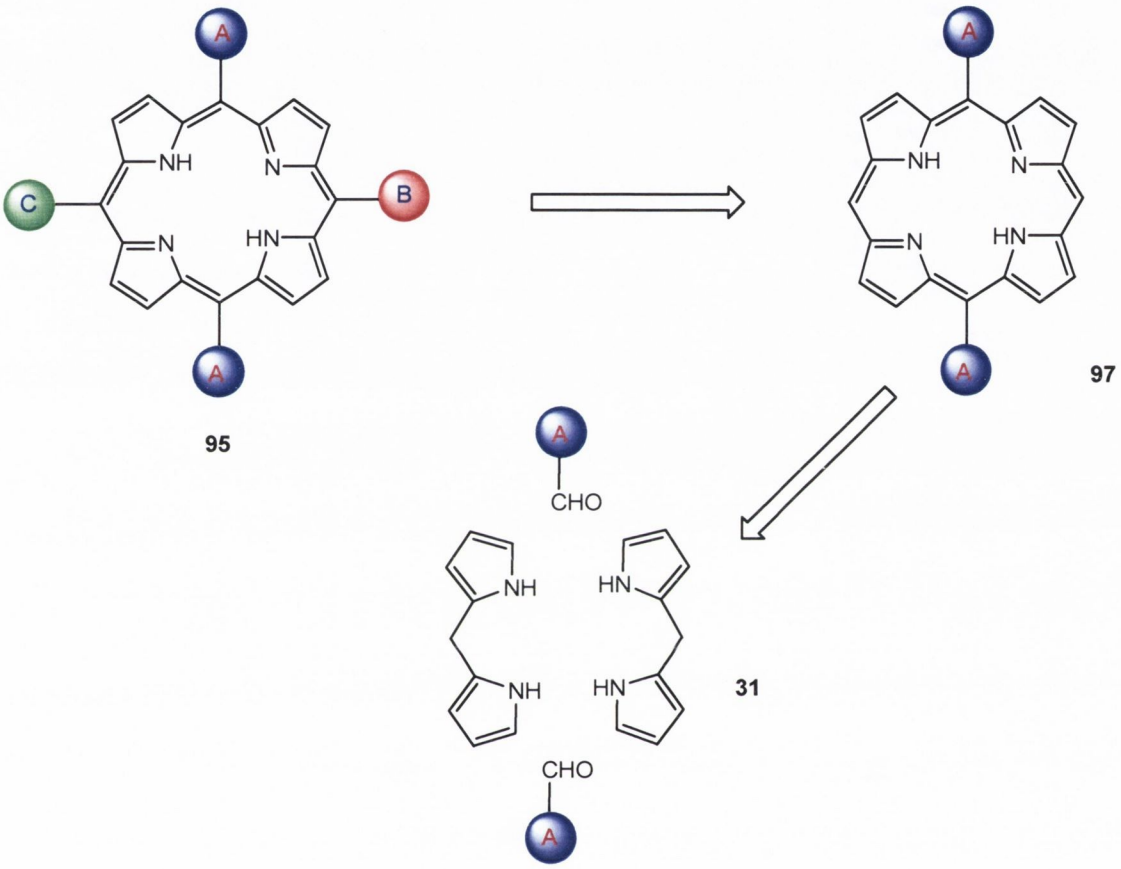
Scheme 3.2. Standard reaction of free base 5,15-A_2-porphyrins with R^2Li/R^3I.

octaethylporphyrin derivatives, it was shown that thermodynamic control of the reaction with RLi results in the predominant formation of oxidation-resistant porphodimethenes.[57,58,103] This requires the intermediary formation of a porphodimethene anion capable of reaction with electrophiles (such as alkyl iodide reagents), while kinetic control of the reaction appeared to proceed *via* a nonnucleophilic phlorin.[64] Thus, it appeared feasible to achieve a disubstitution of free base porphyrins with both nucleophiles and electrophiles under thermodynamically controlled conditions.

The basic retrosynthetic approach for various functionalized tetra-(A_2BC-type) meso-substituted unsymmetric porphyrins **95** by the new method is illustrated in Scheme 3.3.

From Scheme 3.3, it is evident that the rational synthesis of A_2BC free base porphyrins **95** has to start with the respective meso disubstituted porphyrin A_2-type free base porphyrins **97**

which are easily accessible *via* a [2 + 2] condensation reaction using dipyrromethane **31** and an appropriate aldehyde. Therefore, treatment of **97** with a combination of organolithium and alkyl iodide reagents in dry THF followed by hydrolysis with water and oxidation with DDQ



Scheme 3.3. Retrosynthetic analysis of A_2BC-type porphyrins *via* RLi/RI method.

should give convenient access to A_2BC-type meso-tetrasubstituted free base porphyrins **95** by introducing the "B" and "C" groups in one-pot synthesis.

Clearly, this method should enable us to A_2BC-type free base porphyrins to be prepared without prior separation of the tri meso-substituted porphyrins and also without activation of the porphyrins by metallation.[130]

Reactions of 5,15-diphenylporphyrin **42** with various combinations of RLi/RI in dry THF yielded the meso-tetrasubstituted A_2BC-type free base porphyrins under optimized reaction conditions (Scheme 3.4). The yields were low to moderate in the range of 20 to 45 %. However, this is superior when compared to the yields for related porphyrins derived from mixed condensations or multi-step syntheses (typically ranging from 5 to 20 %).[131-133]

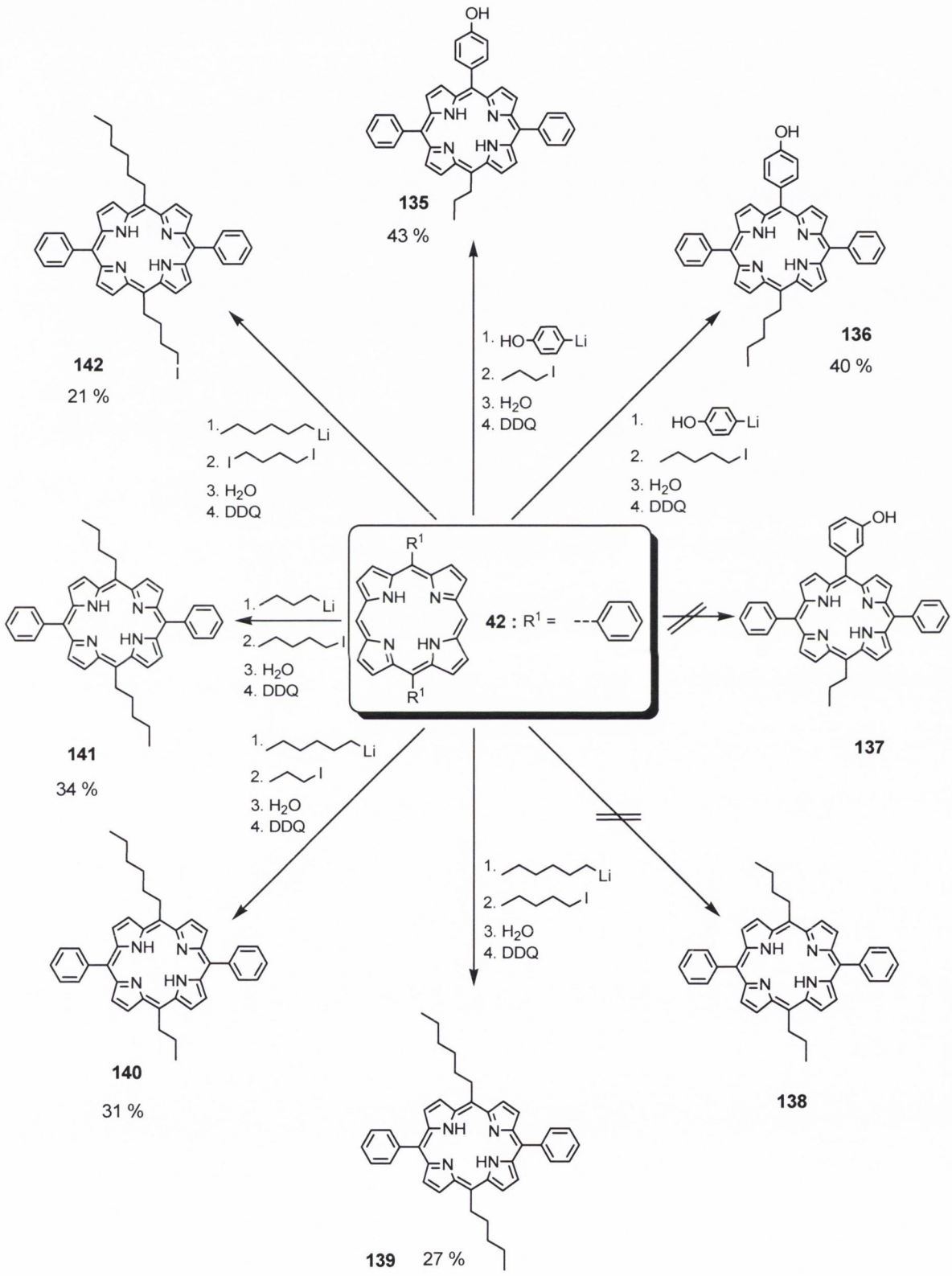
In general, three to four equivalents of organolithium reagents were used and more than ten equivalents of alkyl iodides. In most cases minor amounts of starting material or meso-trisubstituted porphyrins were recovered.

Porphyrin **142** formed by using 1,3-diiodobutane gave the lowest yield (21 %) besides formation of the meso-trisubstituted porphyrin (15 %) and starting material **42** (8 %). The functionalized unsymmetric porphyrins bearing *p*-hydroxyphenyl group **135** and **136** were formed *via* nucleophilic attack of *p*-hydroxyphenyllithium with propyl and pentyl iodides in better yields of 43 and 40 % respectively with separation of minor amounts of only meso-trisubstituted porphyrins in this case. However, porphyrin **137** bearing a *m*-hydroxyphenyl group was not formed and the reaction yielded only the meso-trisubstituted porphyrin. In addition, the A_2BC-porphyrins **139-141** with two aliphatic residues were successfully synthesized. Surprisingly, porphyrin **138** was not formed (Scheme 3.4).

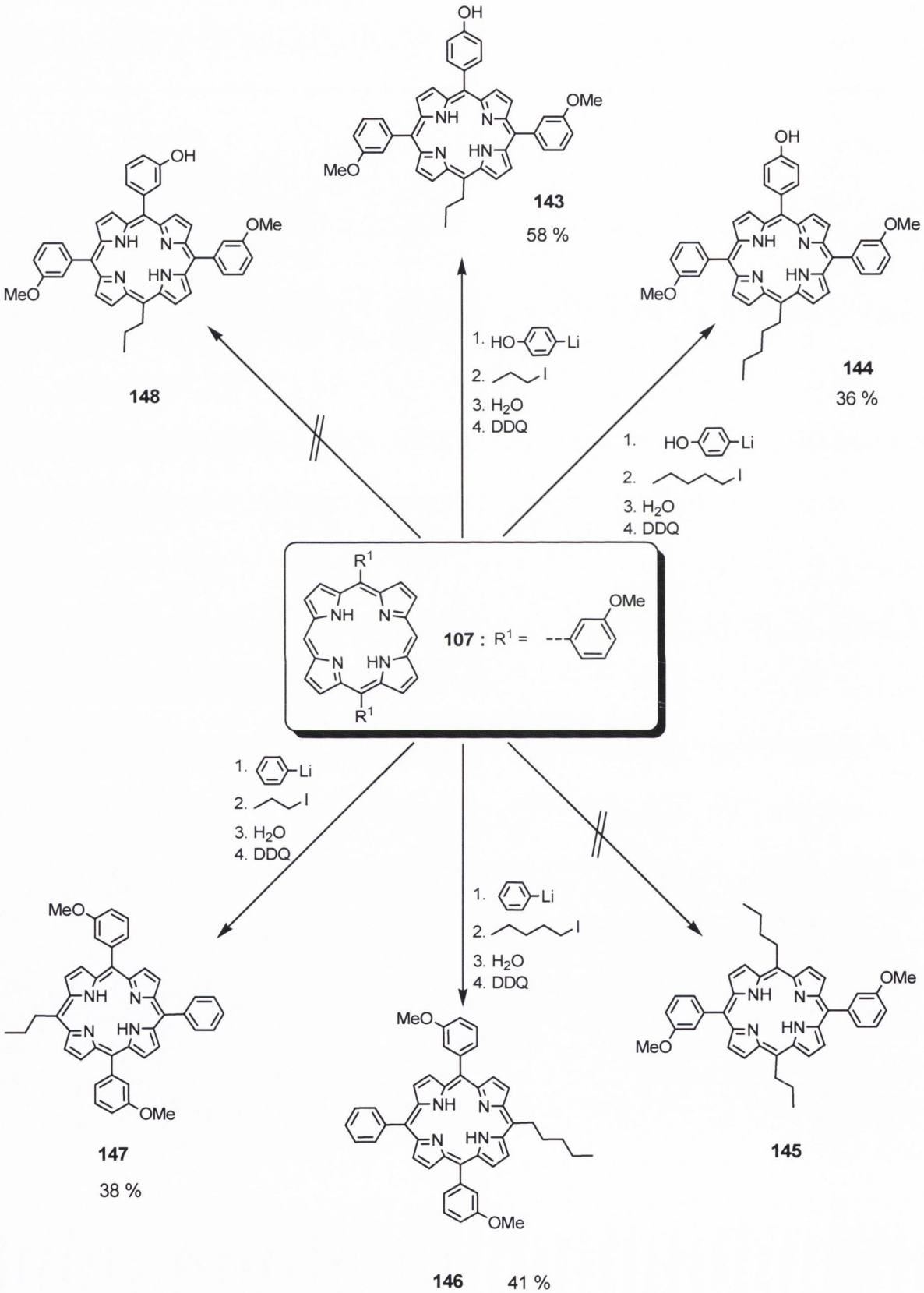
Likewise, reaction of 5,15-bis(3-methoxyphenylporphyrin) **107** with different RLi/RI yielded meso-tetrasubstituted A_2BC-type free base porphyrins under the same optimized reaction conditions (Scheme 3.5). Here, the yields were moderate to good in the range of 35 to 60 %. Indeed, porphyrins (**143**, **144**, **146**, and **147**) bearing *p*-hydroxyphenyl and phenyl groups were formed in good yields by using *p*-hydroxyphenyllithium and phenyllithium with propyl and pentyl iodide reagents. As before, unsymmetric porphyrins **148** and **145** bearing *m*-hydroxyphenyl and butyl group were not formed and the reaction yielded only the meso-trisubstituted porphyrins (Scheme 3.5).

The overall reaction of RLi with the free base porphyrins is a nucleophilic substitution like the Ziegler Alkylation[102] and proceeds *via* initial reaction of organic nucleophile with a meso carbon yielding an anionic species which is hydrolyzed to dihydroporphyrin or can be used as an *in situ* nucleophile for the reaction with alkyliodides, allowing the introduction of two different substituents in a one-pot reaction. Subsequent hydrolysis with water and oxidation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) yields the meso-substituted porphyrins. Key features of the optimized conditions were: (a) using excess RI reagent (more than 10 equivalents; (b) prolonged reaction times under heating (12-24 h at 70 °C) after addition of RI; (c) addition of RI ***prior* to** the hydrolysis step.

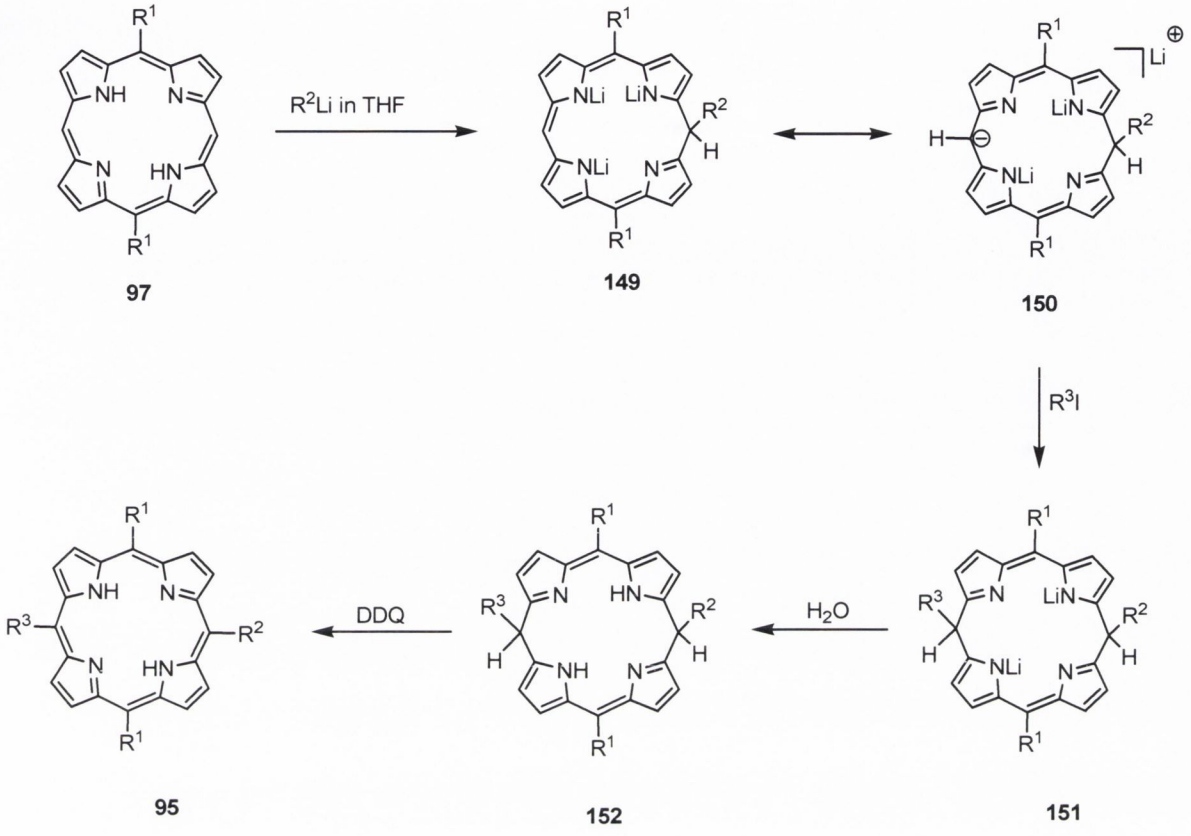
The sequence of the postulated mechanism involves addition of LiR^2 to porphyrin **6** to form the phlorin-type intermediate **149** (Scheme 3.6).



Scheme 3.4. Reactions of 5,15-diphenylporphyrin **42** with various combinations of RLi/RI reagents to afford A_2BC-porphyrins *via* one-pot synthesis.



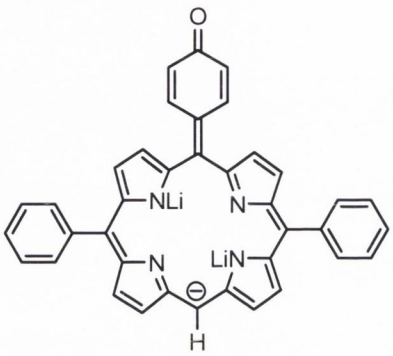
Scheme 3.5. Reactions of 5,15-bis(3-methoxyphenyl)porphyrin **107** with various combinations of RLi/RI reagents to afford A_2BC-porphyrins *via* one-pot synthesis.



Scheme 3.6. Putative reaction mechanism for the one-pot synthesis of A_2BC-type free base porphyrins.

Trapping of the mesomeric carbanionic complex **150** is then achieved by the alkyliodide to form intermediate **151**. Intermediate **149** is believed to have a planar conformation favoring a double bond character at position 20, facilitated by the putative localization[134] of the two lithium ions with attached THF molecules.[64] The more reactive nucleophilic form **150** requires a conformationally distorted sp^3 hybridized meso-carbon atom which is facilitated by steric (*peri* interactions in the octaethylporphyrin series)[135] or metal (Ni—N bond contraction)[136] effects. Presumably, thermal removal of the THF ligands aids in the formation of a conformationally more distorted form with a higher nucleophilic character of meso position 20. Subsequent hydrolysis with water to obtain compound **152** followed by oxidation with DDQ then yields the A_2BC porphyrin **95**. The lower yields of the free base porphyrins **95** compared to the nickel (II) or octaethylporphyrin derivatives described earlier[56,57,63,64,126] reflect the lesser degree of conformational distortion and thus weaker nucleophilic character of **150**. The necessity to effectively stabilize the porphodimethene anion is also reflected in the different yields derived from reaction with various RLi reagents. In line with observations for

porphyrin S_NAr monosubstitution reactions the yields are better with aryllithium reagents than alkyllithium reagents.[58,125] Using alkyllithium/alkyliodide combinations the yields are low to moderate. The best yields were obtained using *p*-hydroxyphenyllithium while the use of *m*-hydroxyphenyllithium resulted in only very small amounts of products (not shown) or in some cases no reaction at all.



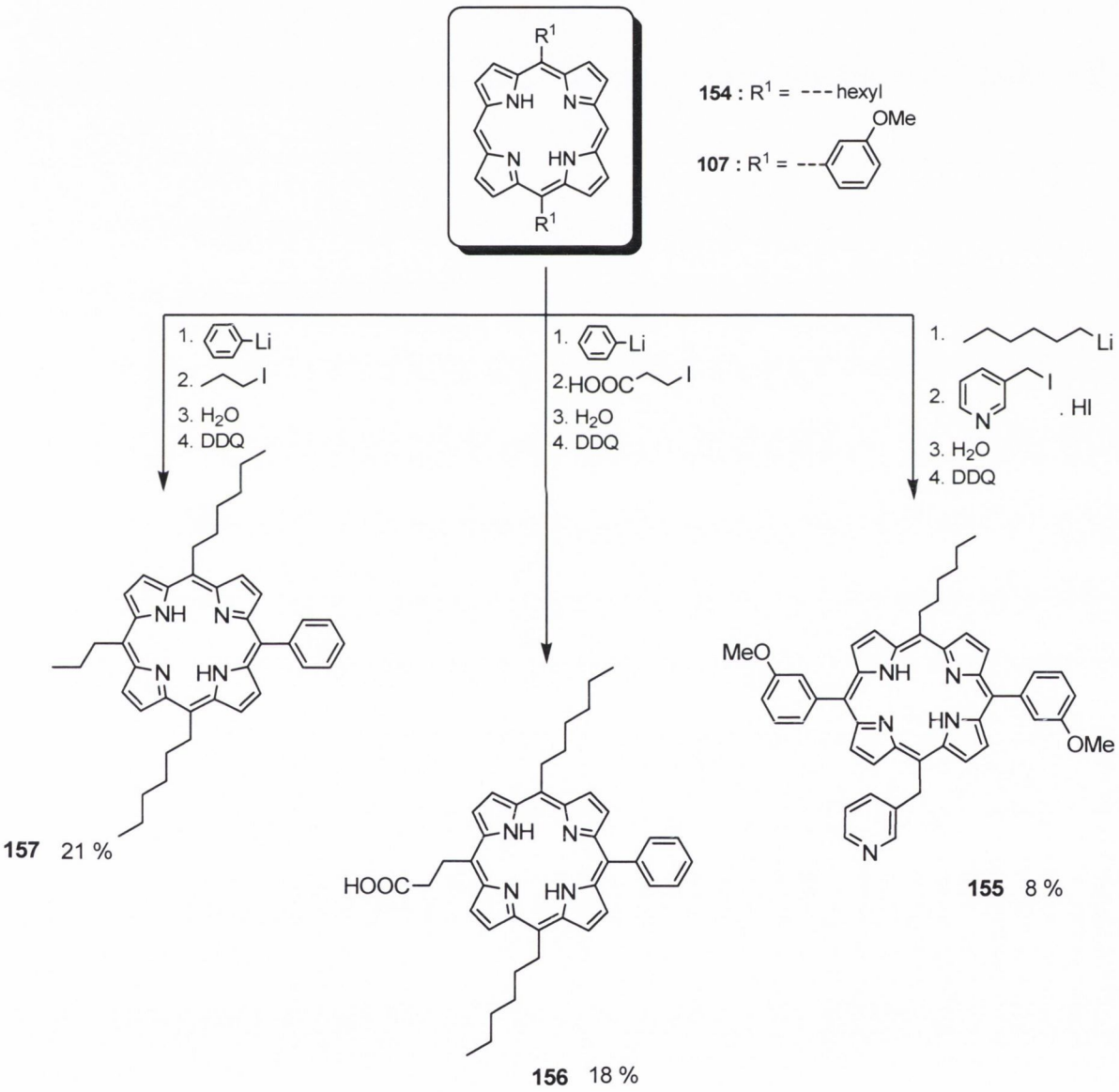
153

Figure 3.1. The quinoid form **153** for *p*-hydroxyphenyl derivatives.

An explanation of the difference in the behavior between the *m*- and *p*-hydroxyphenyl derivatives lies in the formation of **153** for the latter (Figure 3.1). This quinoid form[132] favors a localization of the negative charge at the meso position opposite to the one attacked by the *p*-hydroxyphenyllithium. The lithiated hydroxyphenyl group also offers a convenient entry to various hydrophilic and amphiphilic porphyrins significantly shortening the synthesis of related A_2B- and A_2BC-type porphyrins.[55,120]

Additionally, the reaction is not limited to free base 5,15-diarylporphyrins but also proceeds with free base 5,15-dialkylporphyrins. For example, 5,15-dihexylporphyrin **154** reacts with phenyllithium and propyliodide to give the expected porphyrin **157** in 21 % yield. Similarly, compound **154** reacts with phenyllithium and 3-iodopropionic acid to form porphyrin **156** in 18 % yield (Scheme 3.7). Mass spectra did not give the molecular ion peak for **156** and this is in regard to the other characteraization techniques employed. As the carboxylic group present in 3-iodopropionic acid is prone to react with phenyllithium at room temperature (RT), excess phenyllithium reagent from the first reaction step has to be eliminated before the addition of 3-iodopropionic acid.

The study was extended successfully to the use of iodides on heterocyclic rings such as pyridine ring. Porphyrin **107** and 3-(iodomethyl)pyridine hydriodide, after initial reaction with *n*-hexyllithium, gave the unsymmetric A_2BC porphyrin **155** in 8 % yield (Scheme 3.7).



Scheme 3.7. One-pot synthesis of A_2BC-porphyrins using different iodide reagents.

3.2.1 ^{1}H-NMR studies of selected A_2BC-porphyrins

The synthesis of various A_2BC-type porphyrins allowed a comparative investigation of their NMR spectra. Exemplary, a comparison of the β protons of two of the synthesized A_2BC-porphyrins is given here. 5,15-Dihexylporphyrin **154** (alkyl substituted A_2-type) was used as the standard compound. Porphyrin **154** has two symmetry axis and consequently the pattern of the β-pyrrole protons shows two AB systems for the non-equivalent protons at 9.38 (H2/H8/H12/H18) and 9.55 ppm (H3/H7/H13/H17), respectively, and the two meso protons (H10/H20) exhibit a singlet at 10.14 ppm (Figure 3.2).

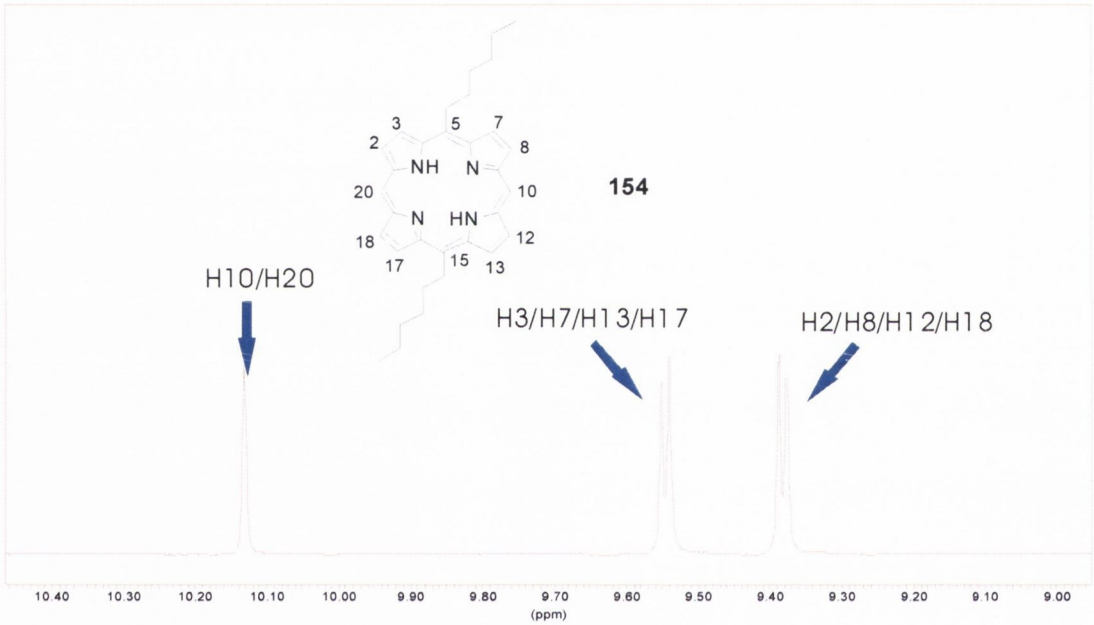


Figure 3.2. ^{1}H NMR spectrum of the β-pyrrole and meso hydrogens of **154** in $CDCl_3$.

The first unsymetrically substituted porphyrin (A_2BC-type) studied was 5,15-dihexyl-10-phenyl-20-propylporphyrin **157** with B as a meso-aryl residue and C as meso-alkyl residue. Porphyrin **157** has only one symmetry axis that passes through the propyl group and the opposite phenyl group (Figure 3.3) and the pattern of the β-pyrrole protons shows three different set of nuclei as two doublets at 8.82 and 9.39 ppm (J = 5.0 Hz) for H8/H12 and H2/H18, respectively and two doublets close in chemical shifts for H3/H7/H13/H17 at 9.52 ppm and 9.56 ppm. As H3/H7/H13/H17 are in proximity to two hexyl groups, they undergo

downfield shift while H8/H12 (in proximity to phenyl group) undergo upfield shifts due to the ring current effect of the phenyl group (Figure 3.3).[121,138-140]

On the other hand, the pattern of the β-pyrrole protons of 5-hexyl-10,20-bis(*m*-methoxyphenyl)-15-[(3-pyridyl)methyl]porphyrin **155** shows three different sets of nuclei as multiplets for H2/H8/H12/H18 at 8.95 ppm and two doublets at 9.33 and 9.48 ppm (J = 5.0 Hz) for H13/H17 and H3/H7, respectively. As H2/H8/H12/H18 are in proximity to two *m*-methoxyphenyl groups, this explains their stronger upfield shift compared to H13/H17 and H3/H7 (Figure 3.4). H3/H7 undergo lower field as they are far from the ring current effect of the *m*-methoxyphenyl or pyridyl groups (Figure 3.4).

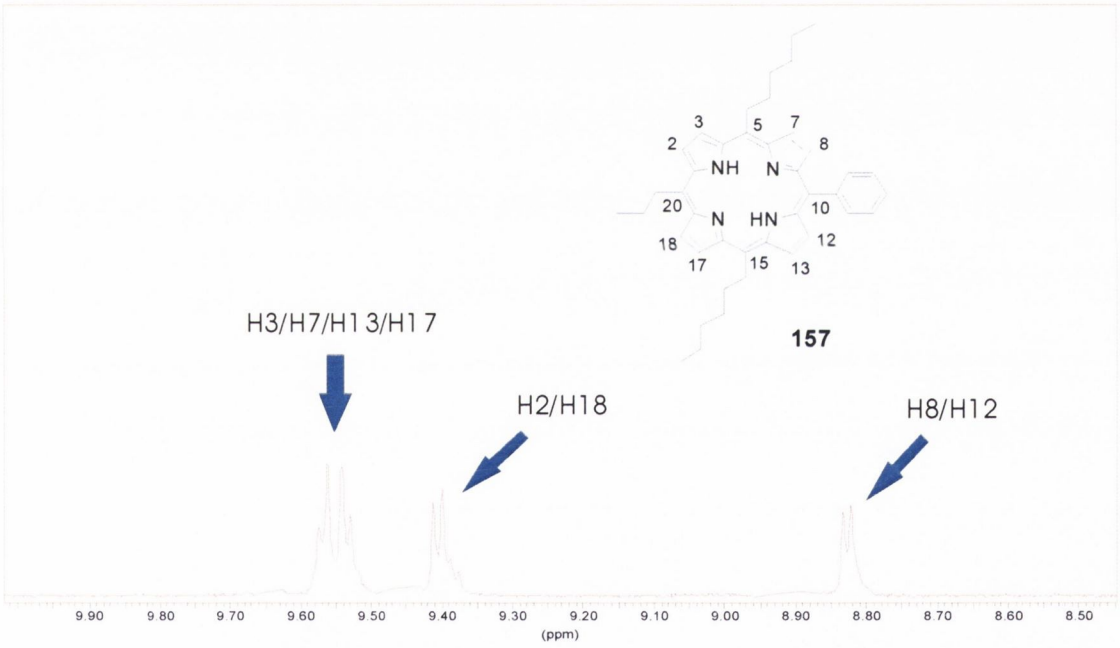


Figure 3.3. ^{1}H NMR spectrum of the β-pyrrole hydrogens of **157** in $CDCl_3$.

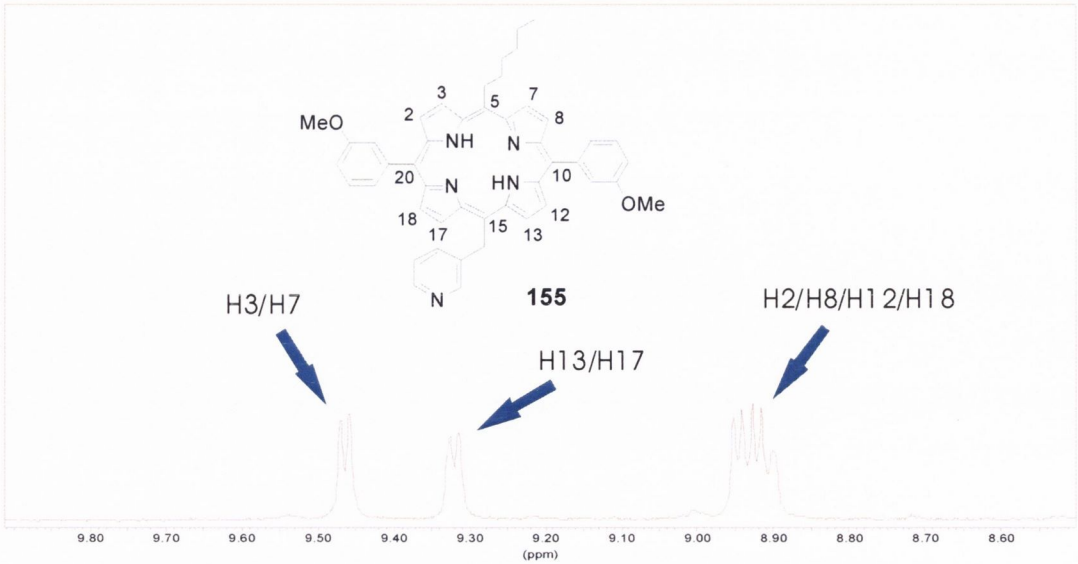
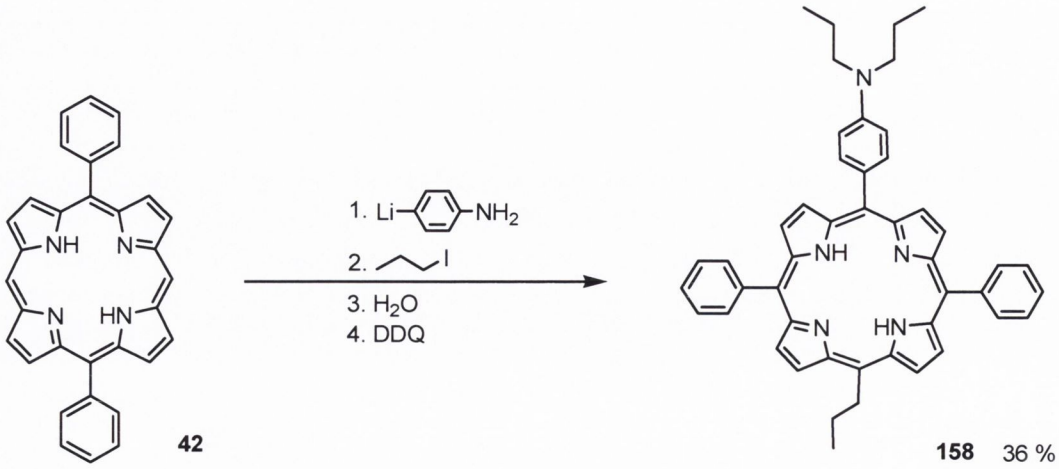


Figure 3.4. ^{1}H NMR spectrum of the β-pyrrole hydrogens of **155** in $CDCl_3$.

3.2.2 Specific classes of A_2BC-porphyrins

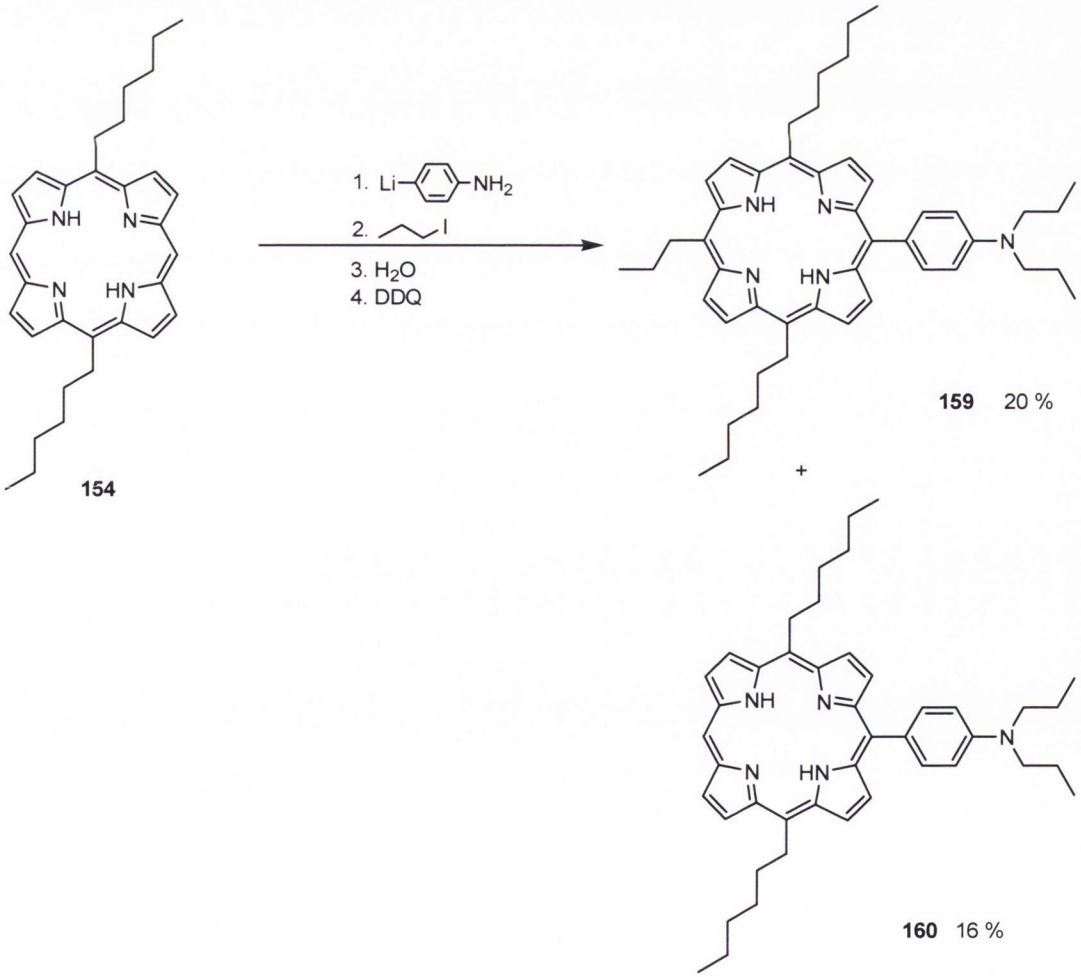
p-Aminophenyllithium proved to be a convenient reagent for the preparation of an interesting class of unsymmetric porphyrins. The reaction of 5,15-diphenylporphyrin **42** with *p*-aminophenyllithium/propyliodide resulted in the formation of porphyrin **158** in 36 % yield (Scheme 3.8). Here four substituents were introduced in a one-pot reaction *p*-aminophenyl group, propyl group at the opposite free meso position and two additional propyl groups *via* dialkylation of the amino group).



Scheme 3.8. Formation of **158**.

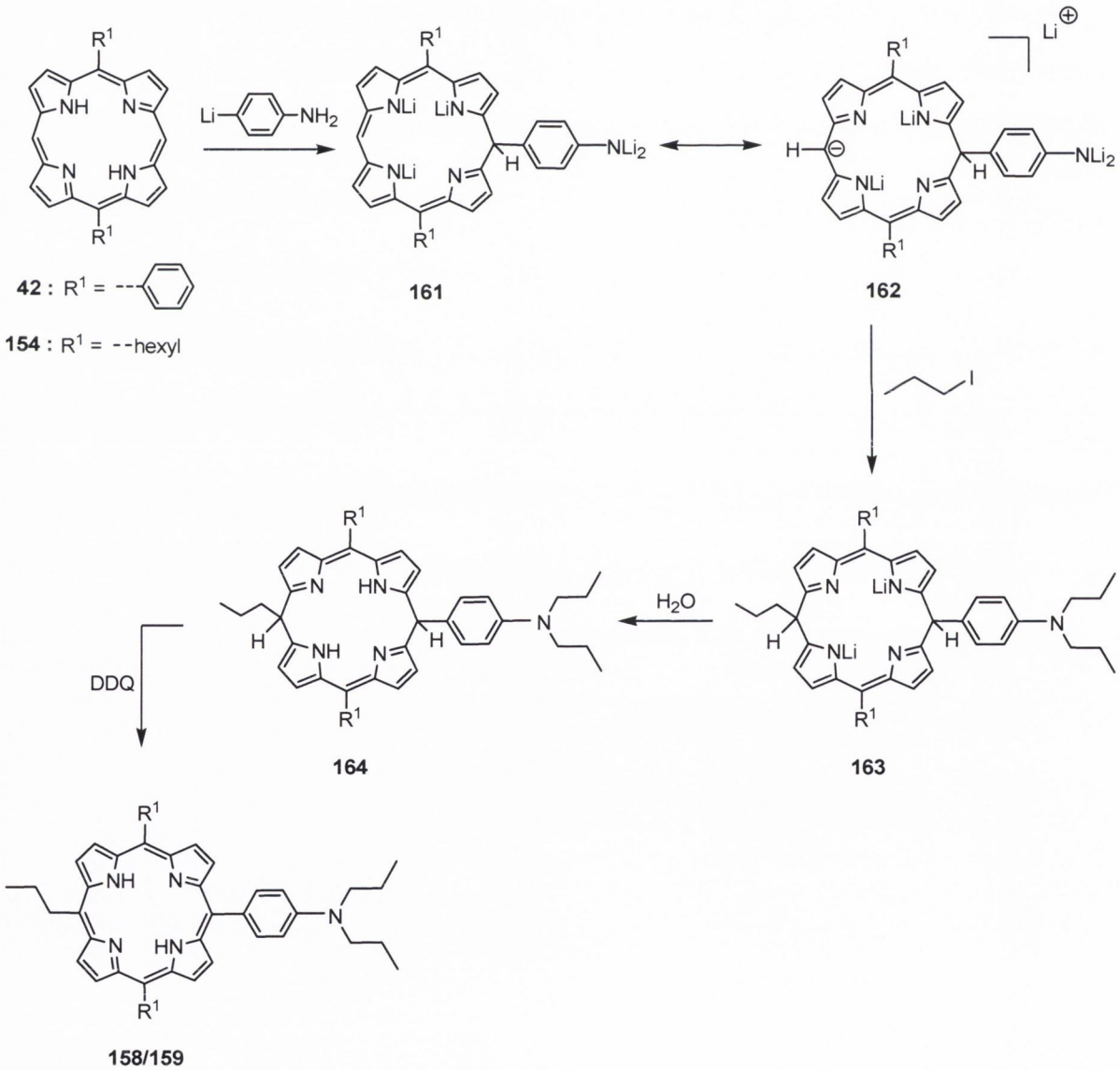
The reaction proceeded with similar success with free base 5,15-dialkylporphyrins. For example, 5,15-dihexylporphyrin **154** reacted with *p*-aminophenyllithium/propyliodide to form porphyrin **159** in 20 % yield (Scheme 3.9). Surprisingly, an A_2B-type porphyrin **160** where introduction of one *p*-aminophenyl group and two propyl groups at the amino group had taken place in this case in 16 % yield.

The mechanism of formation of **158** and **159** was postulated in Scheme 3.10. First, the *p*-aminophenyl residue reacts as a nucleophile with one of the free meso positions forming the phlorin-type intermediate **161** with dilithiation of the two hydrogen atoms in the amino group on the phenyl residue. Trapping of the mesomeric carbanionic complex **162** with the electrophilic propyl group occurs, accompanied by concomitant dialkylation of the intermediary dilithiated amino group to form intermediate **163**. Subsequent hydrolysis with water to obtain compound **164** followed by oxidation with DDQ then yields the A_2BC porphyrins **158** and **159** (Scheme 3.10).



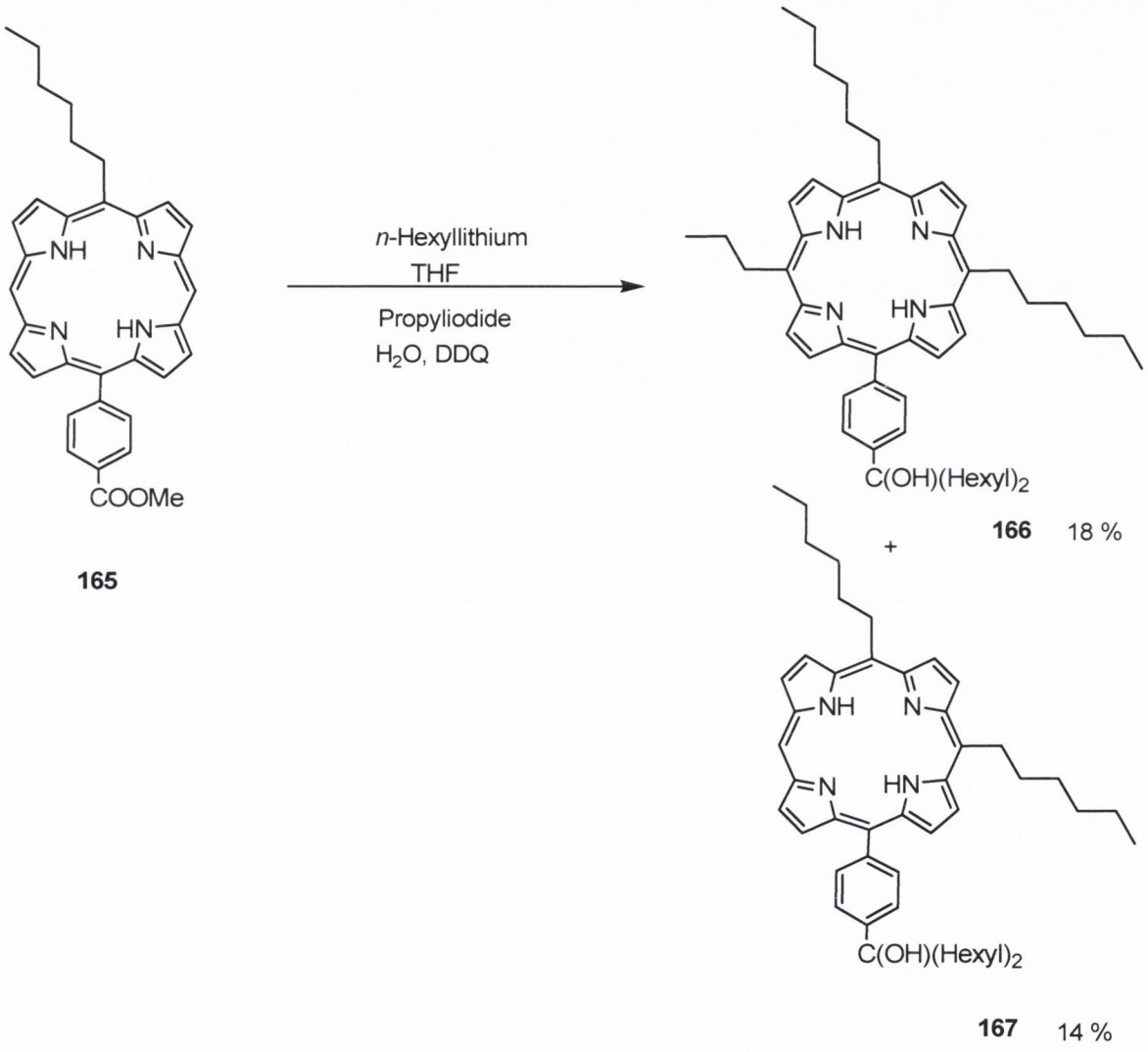
Scheme 3.9. Formation of **159** and **160** *via* reaction of **154** with *p*-aminophenyllithium and propyl iodide.

Subsequently, we intended to broaden the scope of the synthesis of unsymmetric porphyrins to the preparation of 5,10,15,20-A_2BC-type porphyrin with the two "A" groups in the 5 and 10 positions. It was planned to use the 5,15-AB porphyrin **165** was used as a starting material with *n*-hexyl group as A and methyl benzoate ester as B taking into account the possibility of a concomitant reaction of the ester group with alkyllithium reagents. Reaction of **165** with *n*-hexyllithium/propyl iodide resulted in the formation of both the 5,10,15,20-A_2BC-type porphyrin **166** in 18 % yield and 5,10,15-A_2B-type porphyrin **167** in 14 % yield (Scheme 3.11).



Scheme 3.10. Postulated Mechanism of formation of **158** and **159**.

The formation of porphyrin **166** in the above reaction follows a mechanistic pathway similar to that of the general mechanism postulated before in **Scheme 3.6**. It involves an attack of *n*-hexyllithium at the meso position which is accompanied by a concurrent attack of another molecule of *n*-hexyllithium at the carbonyl ester of **165** to form an anionic intermediate to form 5,10,15,20-A_2BC-type porphyrin **166**.



Scheme 3.11. Reaction of **165** with *n*-hexyllithium/propyl iodide.

The pattern of the β-pyrrole protons of porphyrin **167** as 5,10,15-A_2B-type was examined. It is evident from Figure 3.5 that H3/H7/H8/H12 show similar behavior and give a multiplet at 9.54 as they flank the two 5- and 10-hexyl groups. Since only H13 and H17 are in proximity to the phenyl residue, they are shifted to higher field (8.87 ppm). In addition, as the chemical environment of H13/H17 is similar, they overlap and appear as one doublet; but in case of

H2/H18 they appear as two doublets at 9.27 and 9.34 ppm due to the chemical environment being dissimilar. The meso proton H20 exhibit a singlet at 10.03 ppm. The AB-system of the phenyl residue appears as two doublets at 7.80 ppm and 8.21 ppm (J = 7.5 Hz) (Figure 3.5).

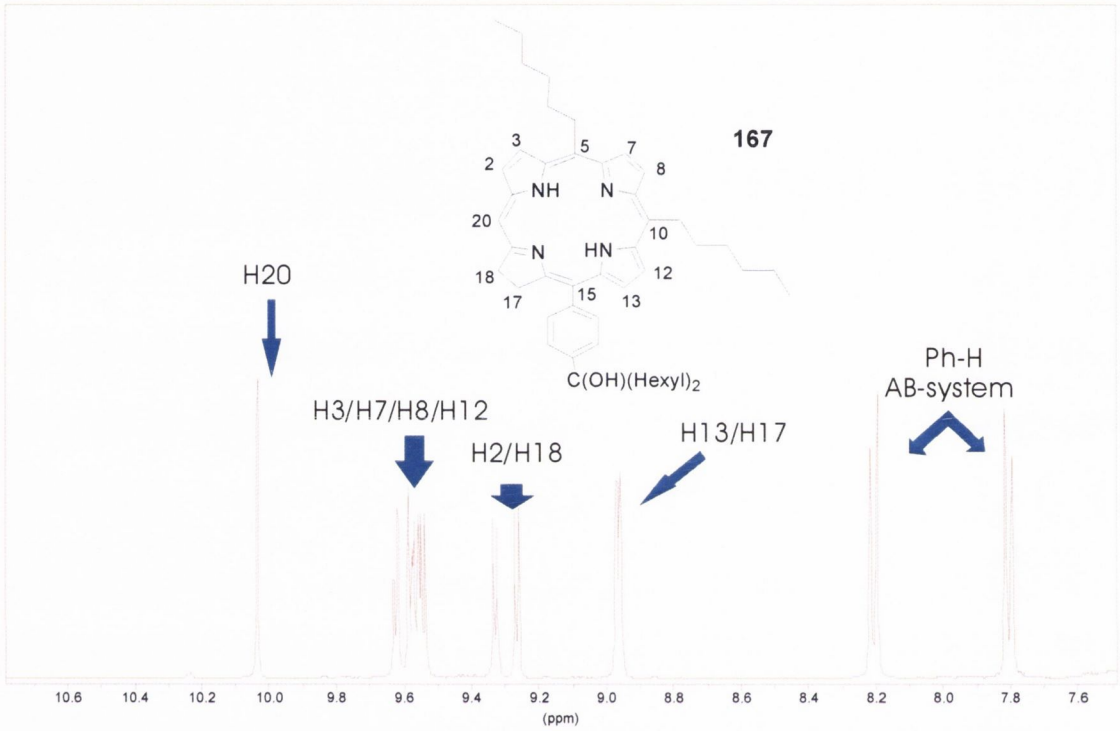


Figure 3.5. ^{1}H NMR spectrum of the β-pyrrole and meso hydrogens of **167** in $CDCl_3$.

The pattern of the β-pyrrole protons of porphyrin **166** (5,10,15,20-A_2BC-type) shows slight differences compared to **167**. From Figure 3.6, it is evident that H3/H7/H8/H12 also show a similar behavior and give a multiplet at 9.54 ppm as the two 5- and 10-hexyl groups are flanked by them. Protons H13 and H17 (closest to the phenyl residue) give doublet at 8.87 ppm. In case of H2 and H18, their chemical shifts overlap, the result being a multiplet at 9.43 ppm rather than the two doublets found in case of H2 and H18 in **167**. This difference is due to the propyl group being situated between them in the 20-meso position which leads to equality of the chemical environment for H2 and H18 (Figure 3.6).

Further proof for the structural assignment was obtained from MS studies. The high resolution mass spectra (HRMS) for the synthesized porphyrins **166** and **167** were completely in agreement with the calculated molecular weight. Porphyrin **167** gave a peak at 753.5416

[M + 1] as shown in Figure 3.7. Porphyrin **166** gave a peak at 795.6022 [M + 1] as shown in Figure 3.8.

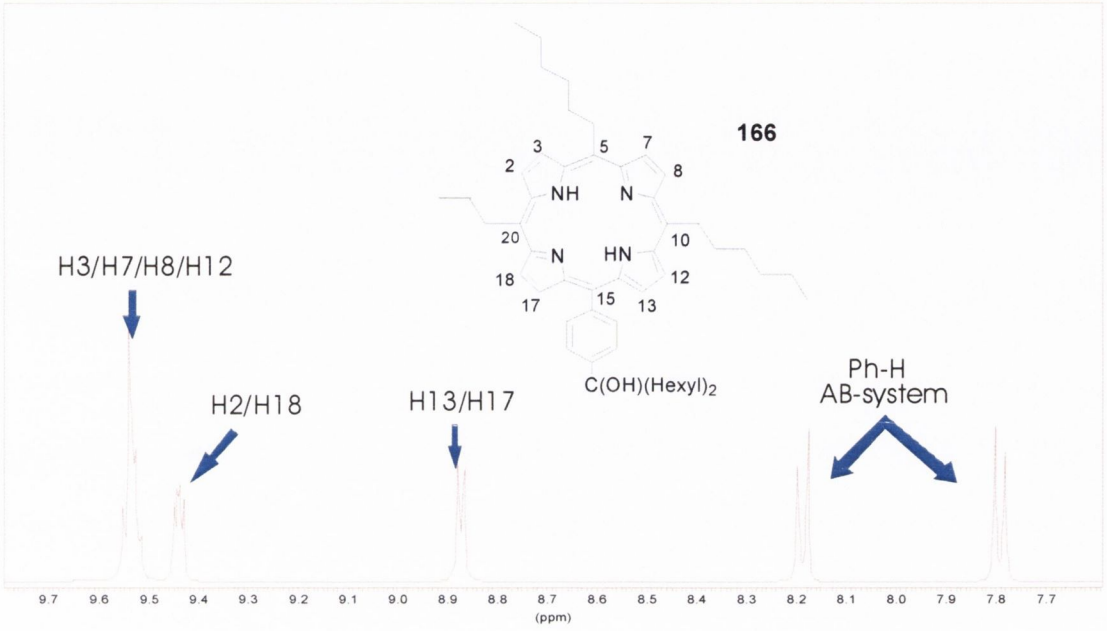


Figure 3.6. ^{1}H NMR spectrum of the β-pyrrole and meso hydrogens of **166** in $CDCl_3$.

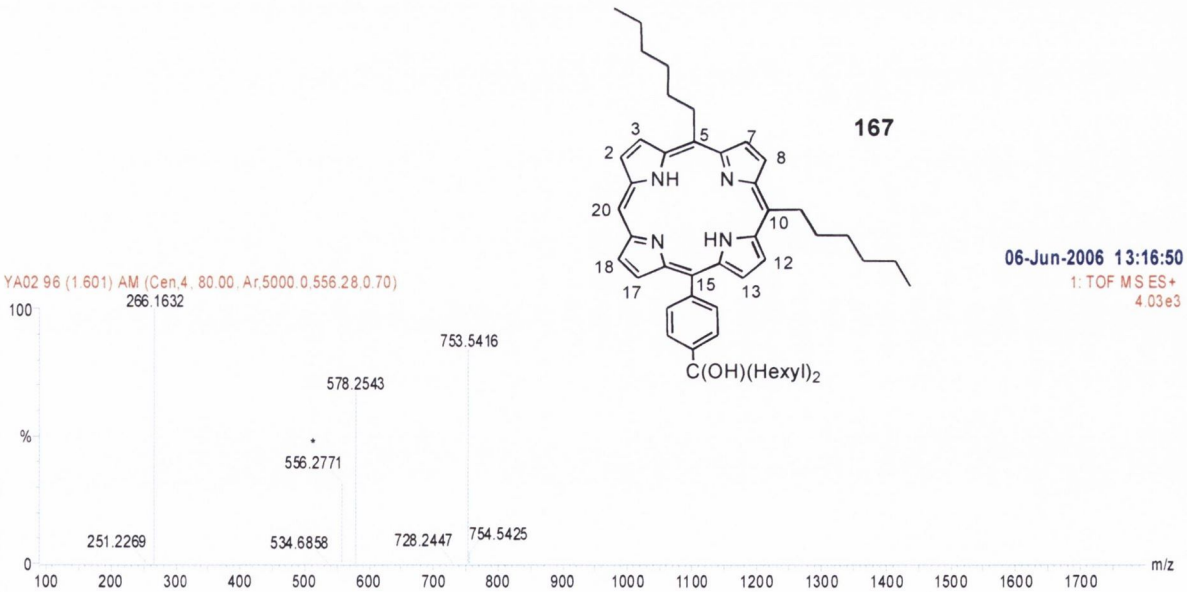


Figure 3.7. HRMS of porphyrin **167**.

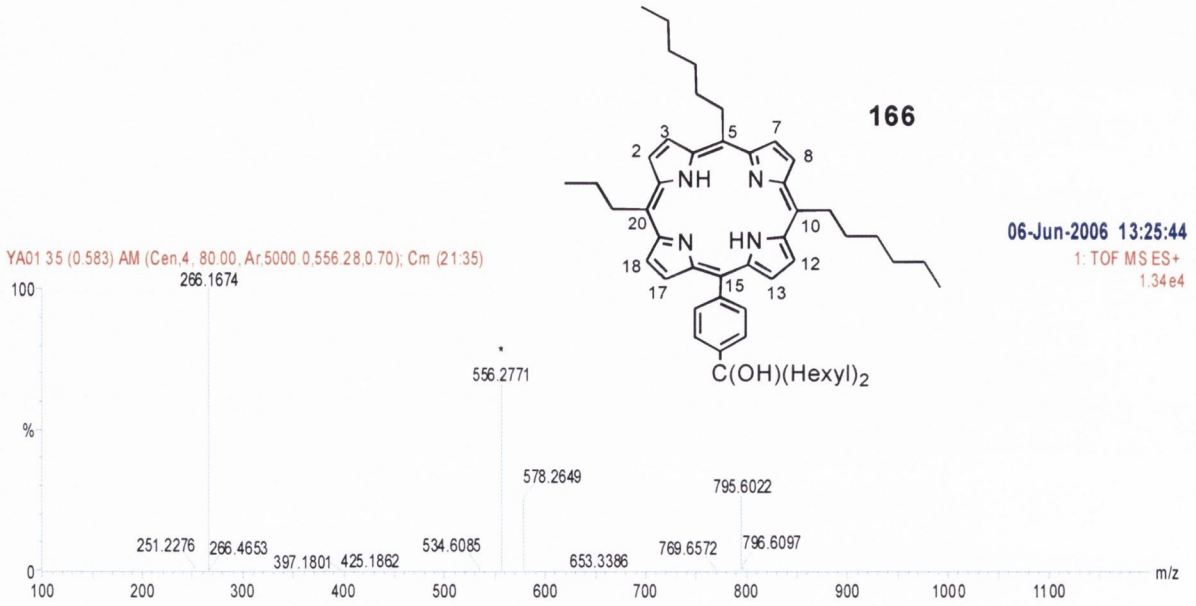


Figure 3.8. HRMS of porphyrin **166**.

3.3 Conclusions

The present methodology complements already established procedures for the a convenient preparation of meso-substituted porphyrins and provides access to meso-disubstituted free base porphyrins in a one-pot procedure while circumventing the use of activated metal complex or the need for metallation-demetallation sequences.

In addition, this new methodology allows the synthesis of various meso-functionalized free base porphyrins *via* disubstitution of two free meso position by a combination of organolithium and iodides reagents in a one-pot reaction and elaborates for functionalization of more complicated macrocyclic systems with β-octasubstituted porphyrins and their metal complexes. Such studies are currently under way in our laboratory.

From a synthetic point of view, these reactions were controlled by optimization of the reaction conditions. The optimal conditions involved heating to 70 °C after the complete addition of the RI reagents, using an excess of RI (more than 10 equivalents), long reaction time with stirring after the addition of the RI reagent (20 — 25 h) and addition of RI before the hydrolysis step.

Mechanistically these reactions are postulated as follow: an addition-oxidation mechanism where the intermediate derived from the free base porphyrin has different electronic nuclear

distributions. The intermediate is believed to be an anionic complex which is reactive towards electrophilic reagents.

Substantial functionalization of the 5,15-disubstituted porphyrins was found by using *p*-aminophenyllithium followed by trapping with an electrophilic reagent accompanied by dialkylation of the intermediary dilithiated amino group.

Finally, the synthetic versatility of organolithium reagents was shown to allow a reaction at both meso positions and carbonyl groups present in the molecule (ketones, aldehydes, acyl halides, esters or carboxylic acids).

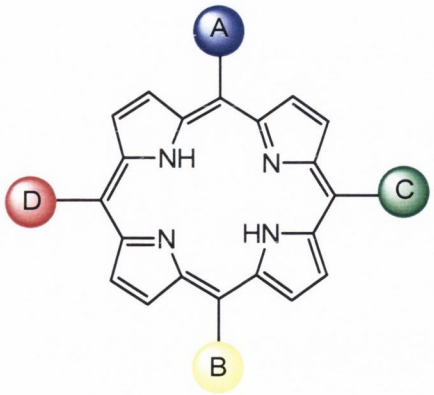
Chapter 4

One-pot synthesis of free base ABCD-type unsymmetrically substituted porphyrins

4.1 Introduction

The synthesis of porphyrins bearing four different meso-substituents, the so-called ABCD-porphyrins **71** remains a challenging topic in porphyrin chemistry (Figure 4.1).[75,131,141] Needless to say that introducing four different substituents with mixed hydrophilic/hydrophopic pattern to the porphyrins would allow a systematic assessment of membrane affinity to establish quantitative structure activity relationships (QSAR) and offers access to new developed photosynthetizers in photodynamic therapy (PDT).

As mentioned in Chapter 1 (Figure 1.4), many studies have been performed for the synthesis of ABCD-porphyrins. All approaches have used stepwise syntheses or mixed condensation reactions. The main problem of the stepwise approach (9-step route starting from pyrrole and carbonyl-containing compounds) is the requirement of multiple synthetic steps to reach the target ABCD-porphyrins[65,79,132,133,142]. Mixed condensations are problematic due to the large number of regioisomers formed, resulting in cumbersome purification and workup (if possible at all).[143] In addition, these reactions involve acid-catalyzed condensation steps, often resulting in significant scrambling of the pyrrole units which limits the types of substituents that can be used. Scrambling must be avoided altogether in the synthesis of ABCD-porphyrins due to the large numbers of possible products.



71

Figure 4.1. ABCD-porphyrin **71**.

Due to these limitations, it was obvious that an alternative approach was desirable. The new approach should require few synthetic steps and not lead to formation of regioisomers so that the necessary purification and workup will be easy.

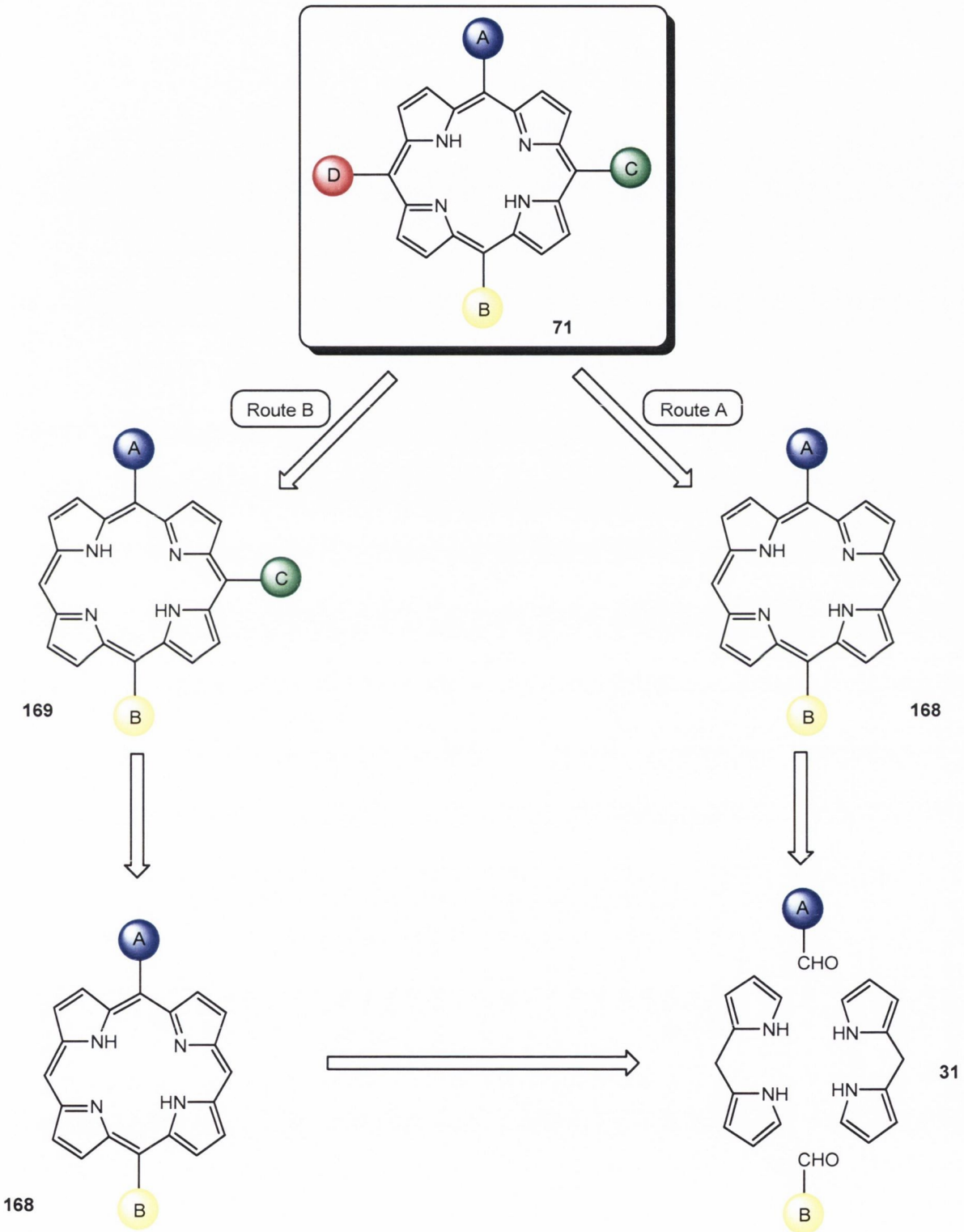
4.2 Results and discussion

In this chapter, we discuss two approaches for the synthesis of ABCD-porphyrin using organolithium reagents and a combination of organolithium reagents with electrophilic iodide reagents which was inspired by the success of the previously described formation of A_2BC-porphyrins from A_2-porphyrins.

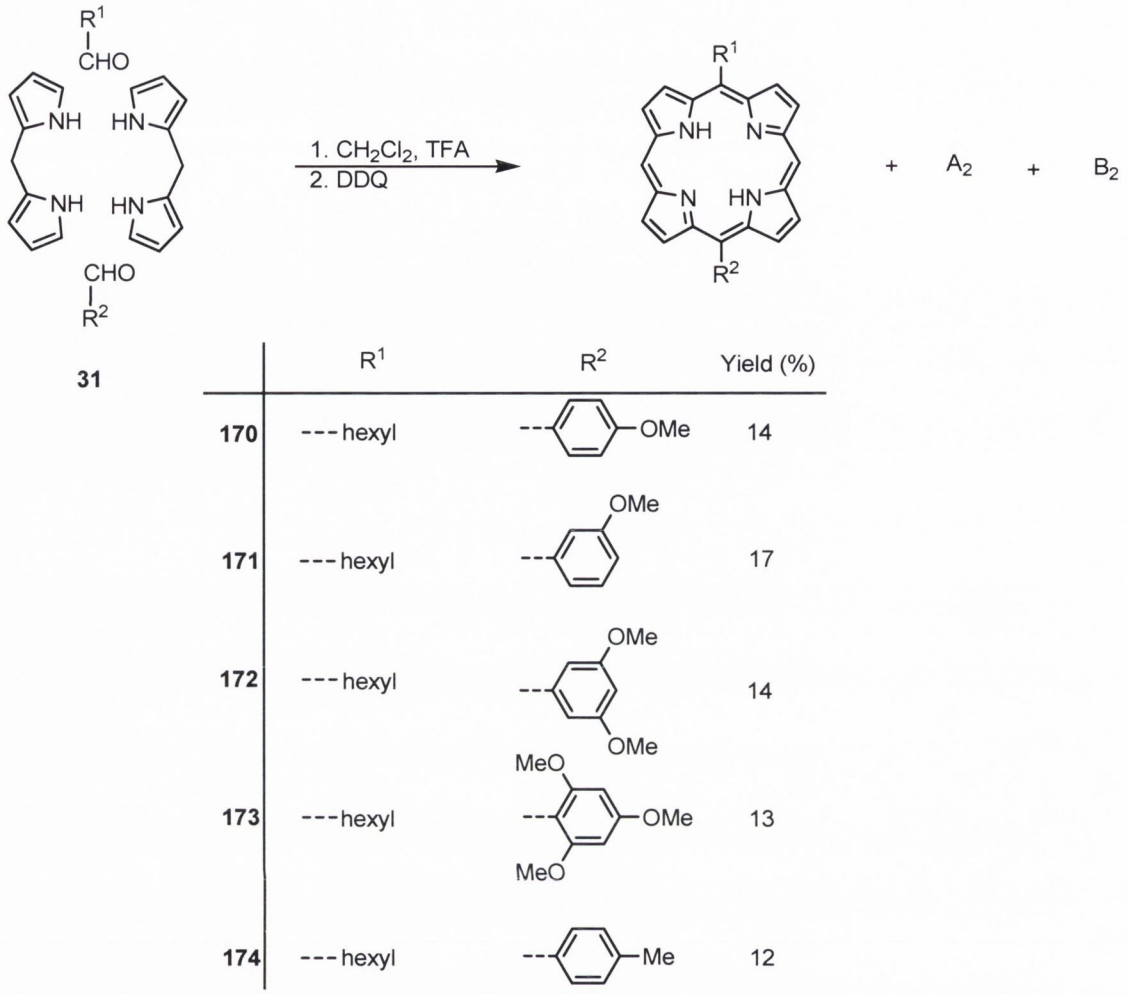
A retrosynthetic analysis for meso-substituted ABCD-porphyris **71** is illustrated in Scheme 4.1. The first possibility for ABCD free base porphyrins **71** starts with the respective meso (AB-type) free base porphyrins **168** which are easily accessible *via* a [2 + 2] condensation reaction using dipyrromethane **31** and two different aldehydes. Therefore, treatment of **168** with a combination of organolithium and alkyl iodide reagents followed by hydrolysis with water and oxidation with DDQ could give convenient access to ABCD-type free base porphyrins **71** by introducing "C" and "D" groups in a one-pot synthesis (Route A).

The second synthetic approach for the synthesis of ABCD free base porphyrins starts also with the respective AB-type free base porphyrins **168**. Thus, ABC free base porphyrins **169** can be prepared *via* reaction of meso disubstituted porphyrin (AB-type) with an appropriate organolithium reagent introducing the "C" group. Further reaction of another appropriate organolithium reagent with meso trisubstituted porphyrins (ABC) **169** introducing the "D" group would afford the desired ABCD porphyrins **71** (Route B).

Initially, we prepared a number of 5,15-AB-type porphyrins (Scheme 4.2). While different methods have been described for these[144] we chose mixed condensations for the first generation of starting materials and prepared compounds **170-174** in yields of 14-20 %. Formation of these AB-porphyrins was always accompanied by formation of the two symmetric A_2 and B_2 porphyrins. The separation of the mixtures was easy in case of 4-methoxy-, 3-methoxy-, 3,5-dimethoxy- or 2,4,6-trimethoxybenzaldehyde as the low solubility of the respective A_2-type porphyrins retained these on the column. Additionally, the resulted AB-type porphyrins (with mixed alkyl/aryl substituents) and B_2-type one (5,15-dihexylporphyrin) always differed significantly in their polarity, thus making a chromatographic separation feasible.



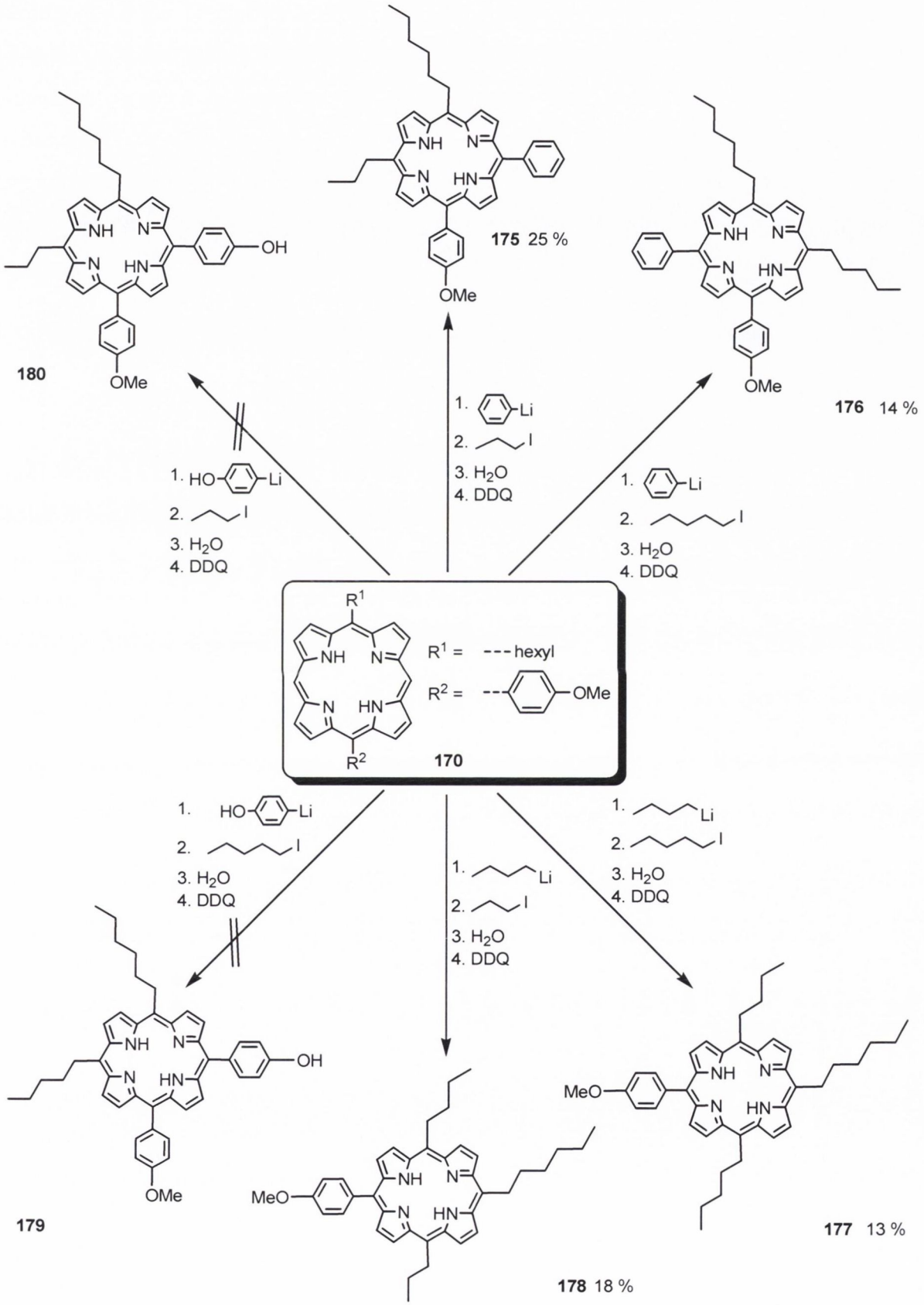
Scheme 4.1. Retrosynthetic analysis of ABCD-porphyrins.



Scheme 4.2. Synthesis of various AB-type porphyrins.

4.2.1 One-pot synthesis of ABCD-porphyrins

Two ABCD-type porphyrins were prepared *via* the one-pot procedure developed for A_2BC-porphyrins. For example, 5,15-disubstituted AB-type porphyrin (5-hexyl-15-*p*-methoxyphenyl-porphyrin) **170** reacted with phenyllithium in dry THF under formation of an anion that can be trapped with alkyliodides (*n*-propyl iodide or *n*-pentyl iodide) under the same optimized reaction conditions as described in Chapter 3 and subsequently be hydrolyzed with water and oxidized with DDQ to the tetra-meso-substituted free base ABCD-porphyrins **175** and **176** in yields of 25 and 14 %, respectively (Scheme 4.3).[63] In a similar manner, the reaction of **170** with *n*-butyllithium/*n*-propyl iodide yielded free base ABCD-porphyrin **178** and reaction with *n*-butyllithium/*n*-pentyl iodide yielded the ABCD- porphyrin **177** in yields



Scheme 4.3. One-pot synthesis of ABCD-porphyrins.

of 18 and 13 %, respectively. In general, three to five equivalents of the organolithium reagents were used and more than ten equivalents of alkyl iodides. Again, complete trapping of the anionic complex formed with electrophiles require long reaction times under heating (12 — 24 h at 70 °C) after addition of the RI. Reaction of **170** with *p*-hydroxyphenyllithium/*n*-pentyl iodide or with *p*-hydroxyphenyllithium/*n*-propyl followed by hydrolysis with water and oxidation with DDQ was expected to yield ABCD-porphyrins **179** and **180**. Surprisingly, the reaction did not go to completion and only the trisubstituted porphyrins were obtained as products (Scheme 4.3).

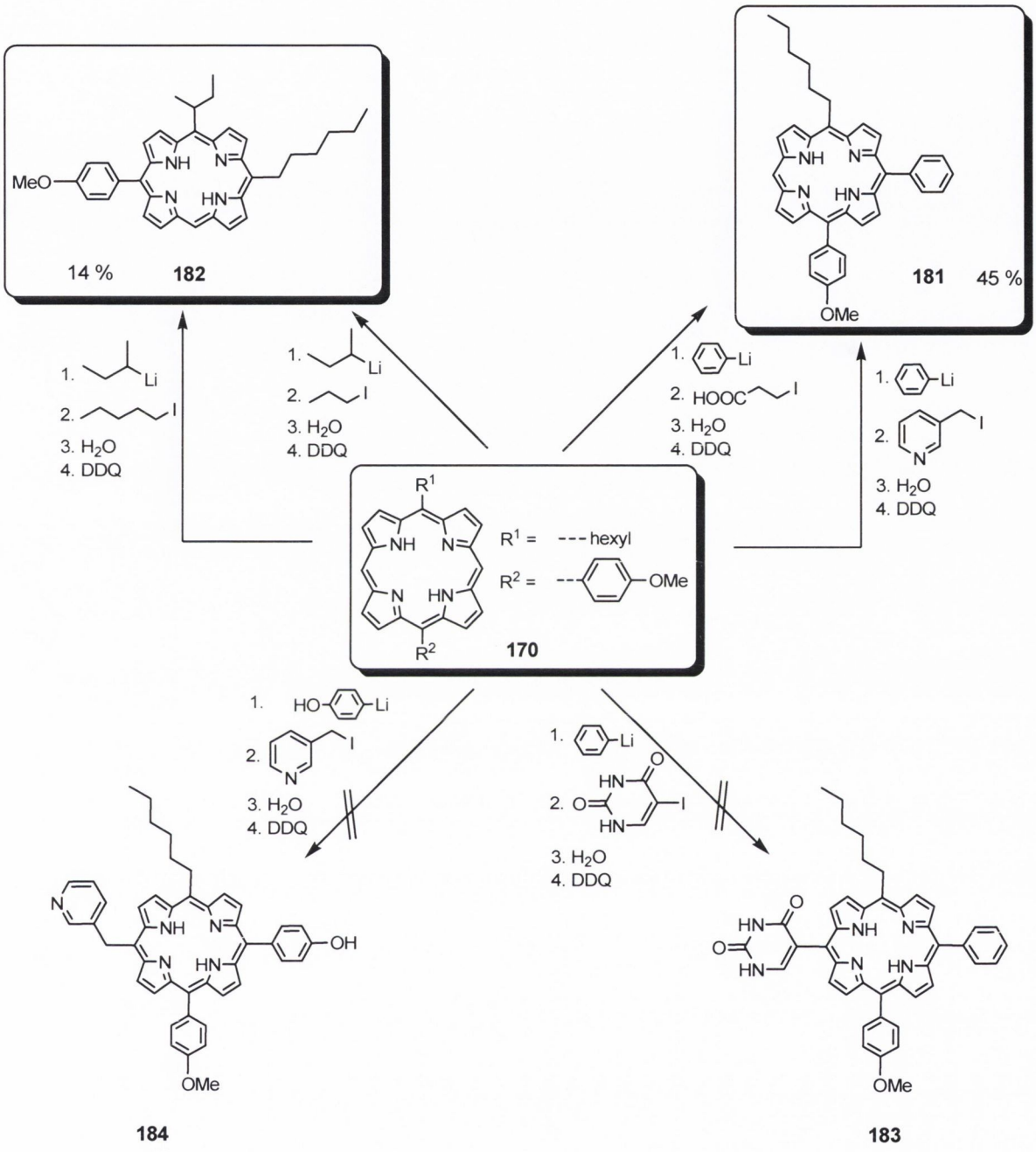
4.2.2 ABC-porphyrin formation

For more detailed studies, similar reactions were performed with 5-hexyl-15-*p*-methoxyphenyl-porphyrin **170** by treating it with various organolithium reagents and different iodide reagents. Reaction of **170** with *sec*-butyllithium/*n*-propyl iodide and with *sec*-butyllithium/*n*-pentyl iodide in dry THF and subsequently hydrolysis with water and oxidation with DDQ yielded the new free base ABC-porphyrin **182** in 14 % yield without any separation of tetra-meso-substituted porphyrins in the two reactions under the optimized reaction conditions described in chapter 3. Similarly, **170** reacted with phenyllithium in dry THF followed by addition of 3-iodopropionic acid or with phenyllithium followed by addition of 3-(iodomethyl)pyridine hydriodide under the same conditions to form ABC-porphyrin **181** in 45 % yield without any formation of ABCD-porphyrins (Scheme 4.4).

In contrast, the reaction of 5-hexyl-15-*p*-methoxyphenyl-porphyrin **170** with phenyllithium/5-iodouracil (dissolved in 2 ml DMF) and with *p*-hydroxyphenyllithium/3-(iodomethyl)pyridine hydriodide in dry THF and boiling the reaction mixture resulted in the formation of polar blue and black materials, indicating ringopening or side product formation. The target ABCD-porphyrins **183** and **184** were not formed (Scheme 4.4).

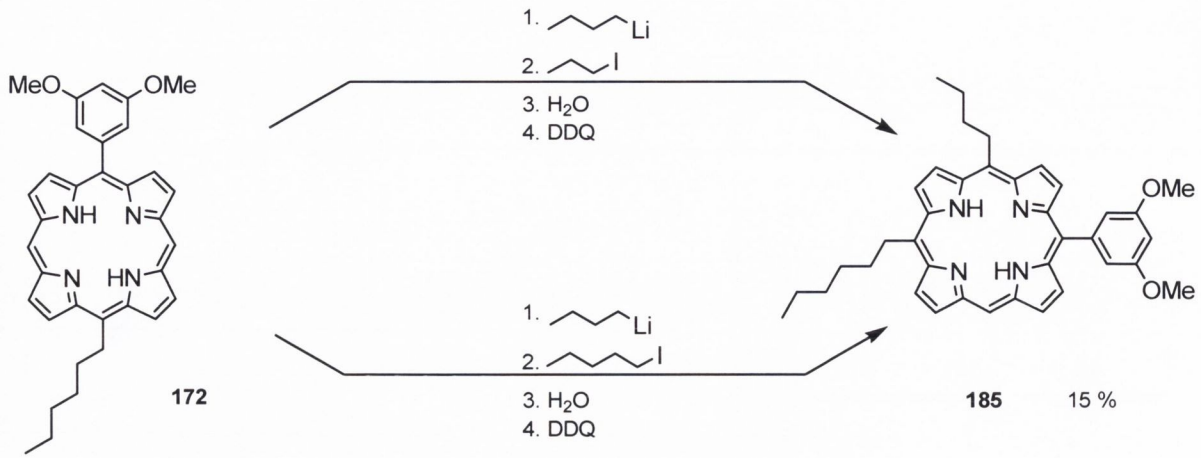
In the next reaction, the AB-type 5-hexyl-15-(3,5-dimethoxyphenyl)-porphyrin **172** was used as starting material. Reaction with *n*-butyllithium/n-propyl iodide and with *n*-butyllithium/*n*-pentyl iodide form the free base ABC-porphyrin **185** in 15 % yield. Again, no ABCD-porphyrin was formed (Scheme 4.5).

Various combinations of organolithium reagents and alkyl, aryl or heterocyclic iodides together with a wide varity of AB-porphyrins with different functional groups (Scheme 4.2) were tested for the synthesis of ABCD-porphyrins. Unfortunately, the experiments failed to

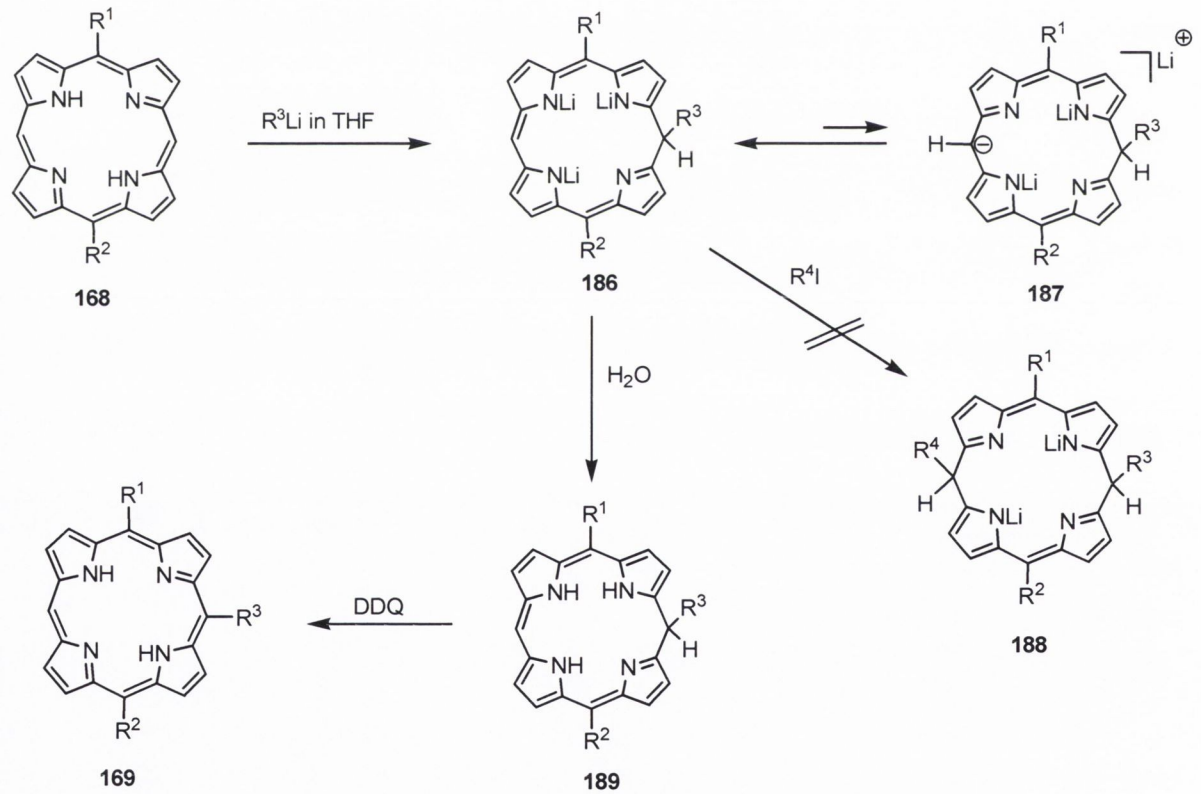


Scheme 4.4. Reactions of **170** with RLi/RI combinations.

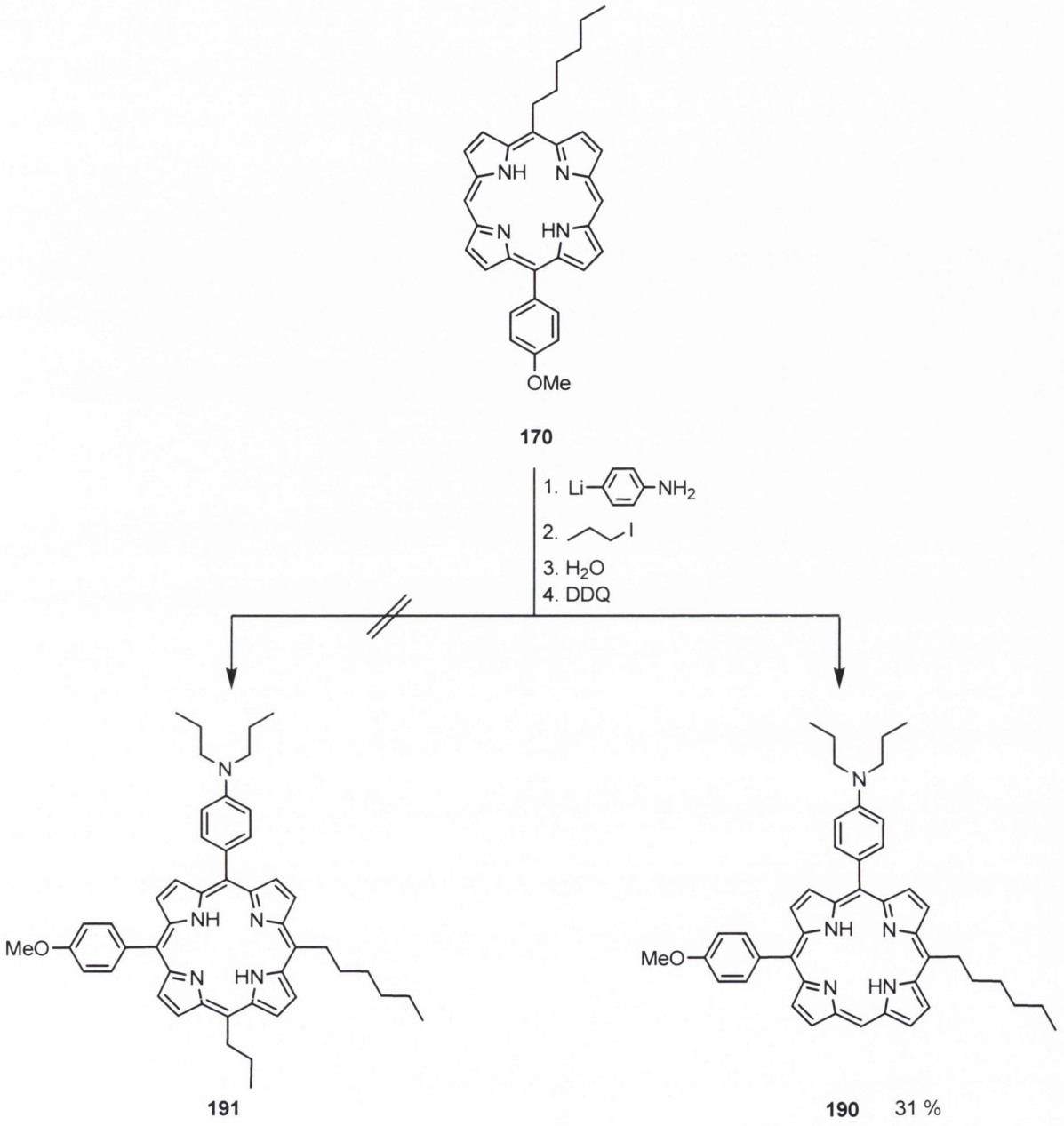
provide the desired product (ABCD-porphyrins) due to various reasons. In some cases probably because of the inability of the *in situ* formed ABC-porphyrin intermediate to react with the electrophilic iodide reagents.



Scheme 4.5. Reactions of **172**.



Scheme 4.6. Putative mechanism of formation of ABC-porphyrin.



Scheme 4.7. Reaction of **170** with *p*-aminophenyllithium.

As shown in the postulated mechanism (Scheme 4.6), the position of the equilibrium was shifted from the carbanionic intermediate **187** to the phlorin type intermediate **186**[134] which is hydrolyzed by water to form **189** followed by oxidation with DDQ to form the free base ABC-porphyrin **169.** Thus, an electrophilic attack of RI to the phlorin type intermediate **186** was hindered due to the low electron density on the free meso position.

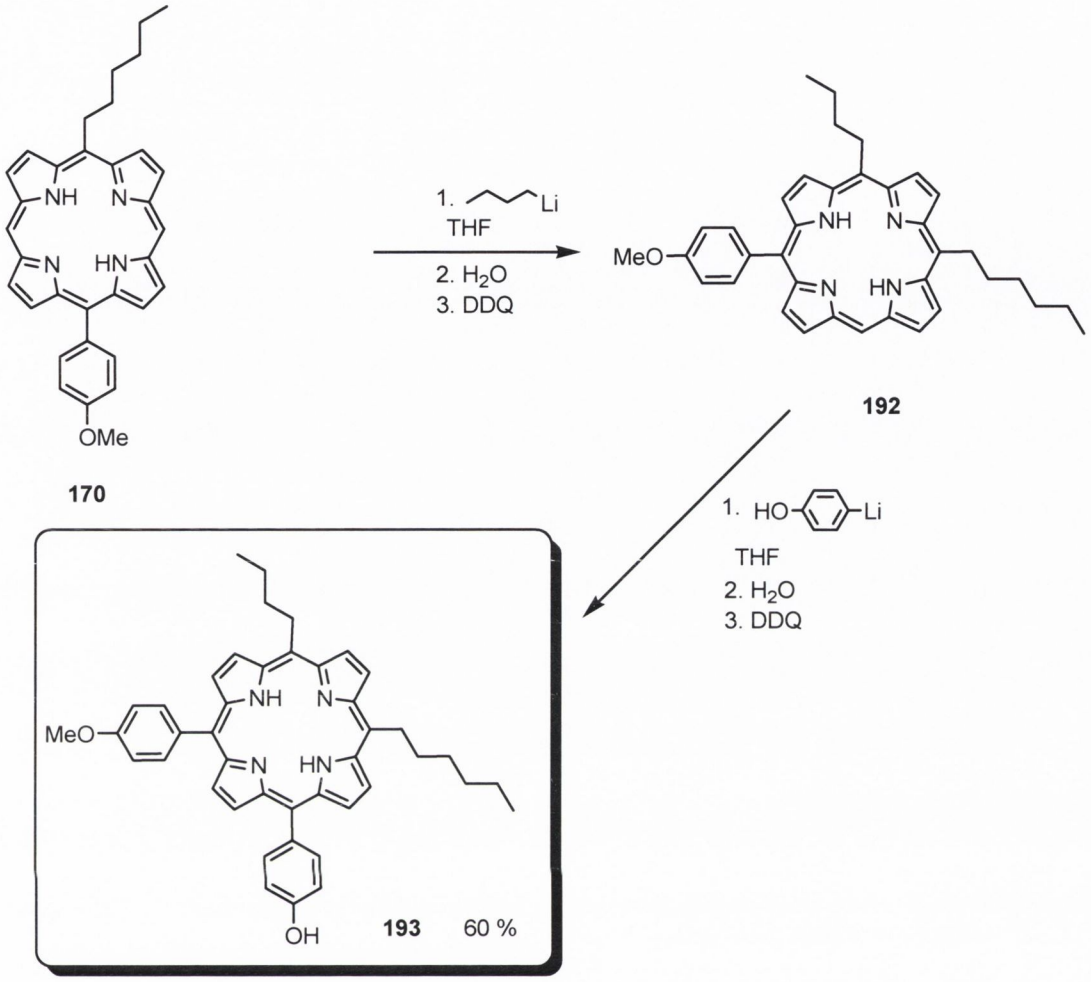
A similar behaviour of AB-type porphyrin was found in reactions with *p*-aminophenyllithum towards AB-type porphyrin has taken a considerable interest. The 5-hexyl-15-*p*-methoxyphenyl-porphyrin **170** was reacted with *p*-aminophenyllithium followed by addition of *n*-propyl iodide and subsequent hydrolysis with water and oxidation with DDQ and yielded the ABC-porphyrin **190** in 31 % yield whose dialkylation of amino group had taken place. Again, no ABCD-porphyrin **191** was formed (Scheme 4.7).

Thus, this reaction proceeds *via* the same mechanism as shown in Scheme 4.6 with the addition of the amino dialkylation.

4.2.3 ABCD-porphyrins via two-step synthesis

Next, we attempted the preparation of ABCD-type porphyrins *via* two-step synthesis through functionalization of the respective AB-porphyrins by S_NAr reactions with organolithium reagents.[62] The two different target compounds were ABCD-porphyrins carrying both precursors for *p*-hydroxyphenyl group and various alkyl chains; compounds with residues in line with our intended biological studies.

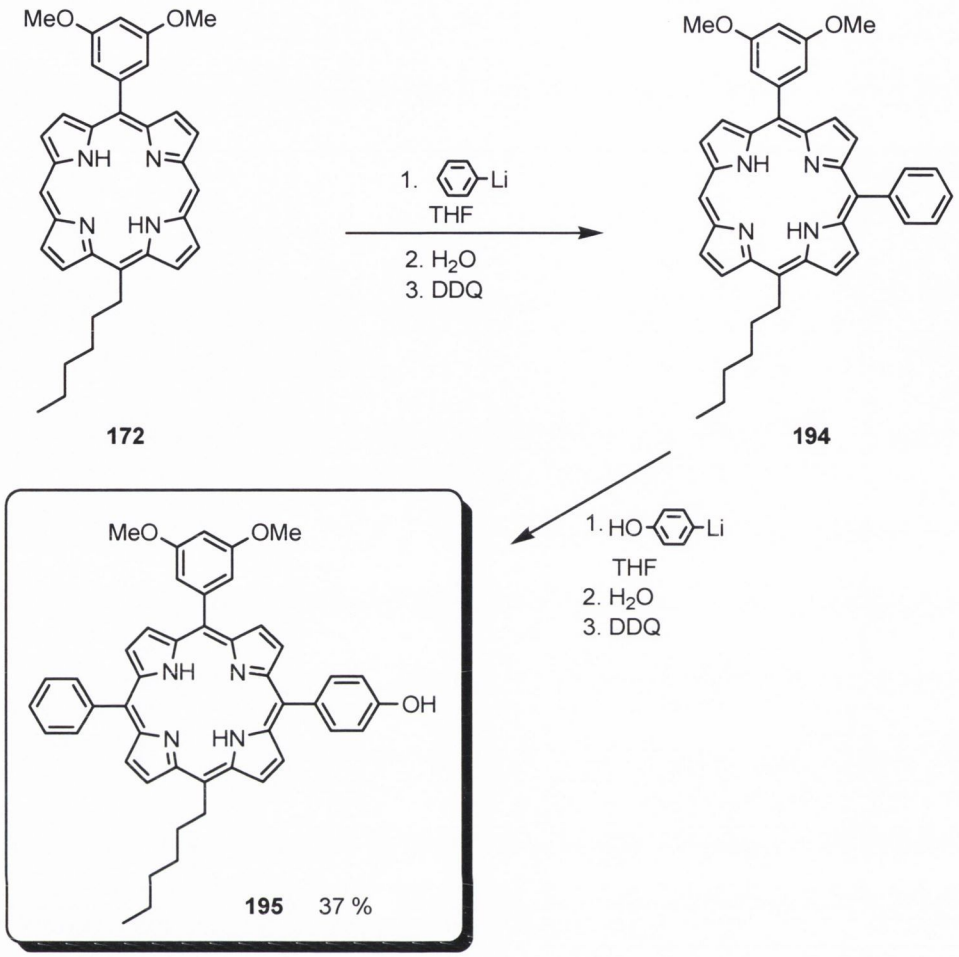
As outlined in Scheme 4.8, the AB-type free base porphyrin **170** reached to ABC-porphyrin **192** *via* addition of *n*-butyllithium to **170** in dry THF and subsequent hydrolysis with water followed by oxidation with DDQ. Compound **192** was not characterized and then added directly to a solution of *p*-hydroxyphenyllithium followed by addition of water and DDQ to form the ABCD-porphyrin, 5-butyl-10-hexyl-15-*p*-hydroxyphenyl-20-*p*-methoxyphenyl-porphyrin **193**, in 60 % yield.



Scheme 4.8. Two step synthesis of the ABCD-porphyrin **193**.

This indicated that this two-step synthesis might be the method of choice for the preparation of functionalized ABCD-porphyrin in acceptable yields as the complete synthetic pathway gave higher overall yields compared to the one-pot procedure.

Secondly, further reactions to elaborate this strategy were achieved. The next reaction involved reaction of AB-type porphyrin **172** with phenyllithium forming the ABC-porphyrin **194** which was not characterized and reacted directly with *p*-hydroxyphenyllithium and gave the ABCD-porphyrin **195** in 37 % yield (Scheme 4.9).



Scheme 4.9. Two step synthesis of the ABCD-porphyrin **195**.

4.2.4 ^{1}H-NMR spectroscopy of AB-, ABC- and A_2BC-porphyrins

The investigation and comparison of the NMR spectra of the β protons of some of the synthesized AB-, ABC-, ABCD-porphyrins was quite interesting. 5-Hexyl-15-*m*-methoxyphenyl-porphyrin **171** (AB-type) is taken as the standard compound. It has one axis of symmetry as shown in Figure 4.2 and the pattern of the β-pyrrole protons shows four AB systems for the non-equivalent protons at 9.16 (H13/H17), 9.38 ppm (H12/H18), 9.46 (H2/H8), 9.65 ppm (H3/H7), respectively, and the two meso protons (H10/H20) exhibit a singlet at 10.27 ppm (Figure 4.2).

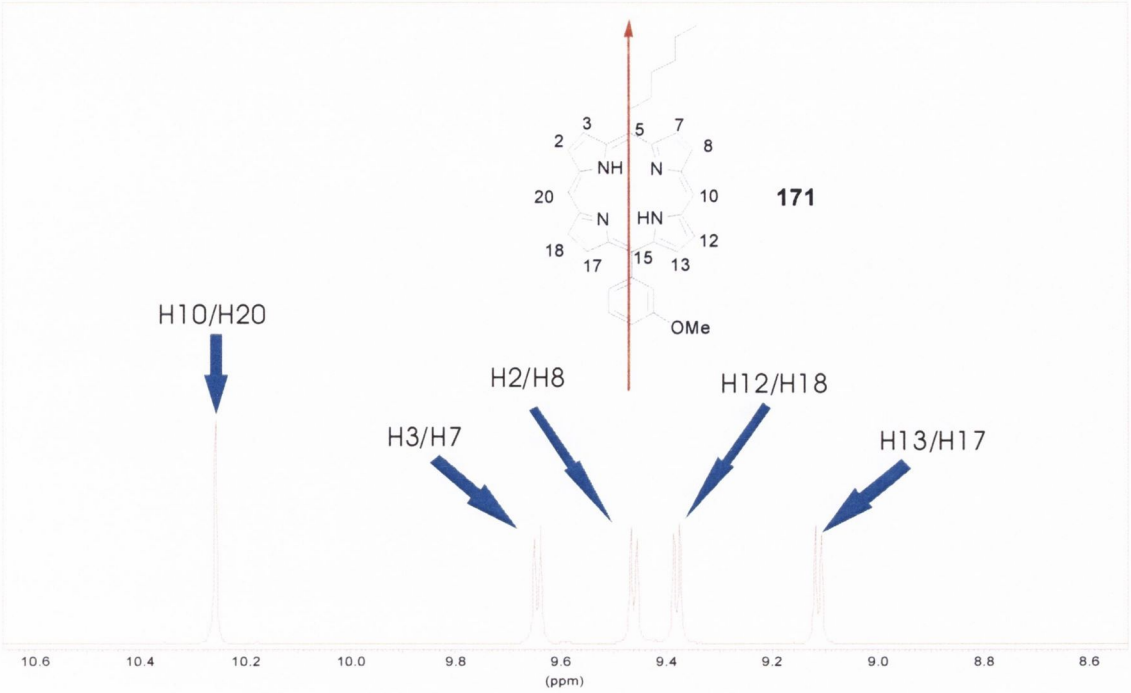


Figure 4.2. ^{1}H NMR spectrum of the β-pyrrole and meso hydrogens of **171**.

The pattern of the β-pyrrole protons of 5-butyl-10-(3,5-dimethoxyphenyl)-20-hexylporphyrin **185** is presented as an example of the ABC-type. Figure 4.3 shows that the β-pyrrole protons pattern of porphyrin **185** looks somewhat like that of porphyrin **167** in Figure 3.5 (Chapter 3). The β-pyrrole protons H2/H3/H7/H18 gave four doublets but in the same region at 9.52-9.65 ppm as two 5- and 10-alkyl residues are flanked by them. Since only H8 and H12 are in proximity to the phenyl residue, they undergo more of an upfield shift. As the chemical environment of them is similar, they appear as two doublets with very similar chemical shifts at 9.02 and 9.04 ppm but in the case of H13/H17 they appear as two doublets at 9.23 and 9.34 ppm due to the dissimilar chemical environment. The meso proton H15 gives a singlet at 10.14 ppm (Figure 4.3).

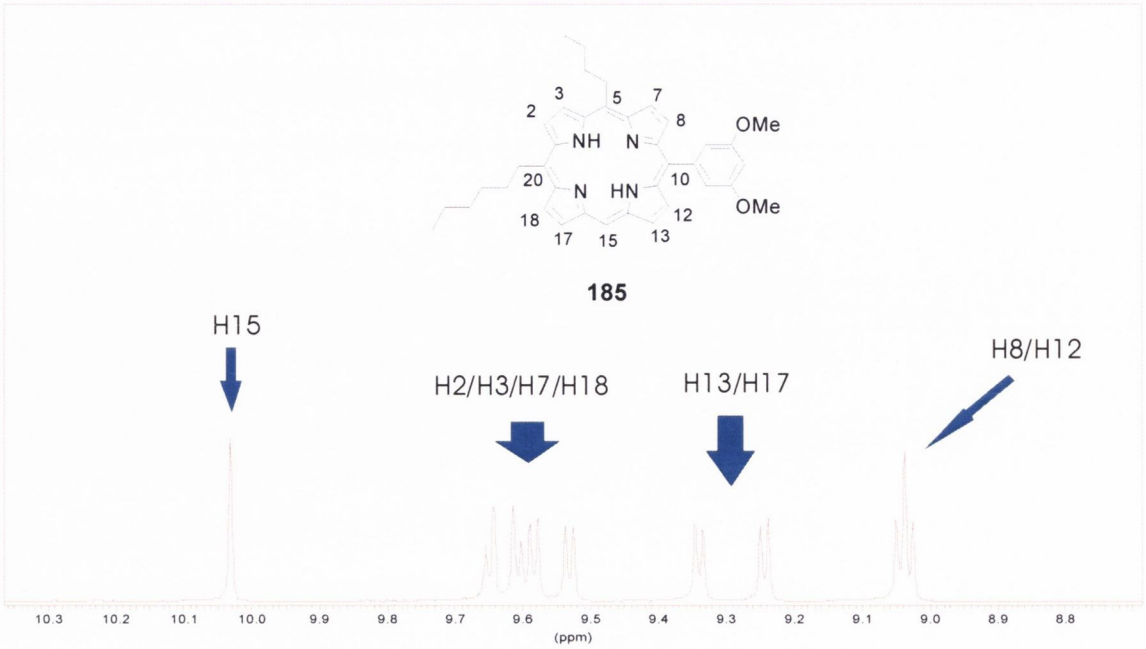


Figure 4.3. ^{1}H NMR spectrum of the β-pyrrole and meso hydrogens of **185** in $CDCl_3$.

A first example for an ABCD-porphyrin was 5-butyl-10-hexyl-15-(4-hydroxyphenyl)-20-(4-methoxyphenyl)porphyrin **193** (with two consecutive aryl and two consecutive alkyl residues). Surprisingly, the ^{1}H NMR spectrum of the β-pyrrole protons gave pattern similar to the aryl 5,10-A_2 or 5,10,15,20-A_2B_2.[59] The spectrum of **193** exhibits two flanking singlets for H17/H18 at 8.78 ppm and H7/H8 at 9.59 ppm and two sets of signals (each as two doublets with very similar chemical shift) for H2/H13 at 8.97 ppm and H3/H12 at 9.45 ppm. While the reported aryl 5,10-A_2 showed a difference in the two sets of signals between the two flanking singlets which appeared as two AB-systems.[59] The similarity in the two flanking signals in **193** compared to 5,10-A_2 indicate than no coupling of the β-pyrrole protons on the same pyrole bearing H7/H8 and H17/H18 is expected. Therefore, despite **193** bears four different substituents, the symmetry of the compound is present because it has two normal alkyl substituents in 5- and 10-meso position and two aryl substituents bearing two oxygens (OH and OMe) in the same positions (*para*) and this give pattern in agreement with the symmetry axis bisecting the two pyrrole bearing H7/H8 and H17/H18 (Figure 4.4).[117]

On the other hand, the spectrum of the β-pyrrole protons in 5-hexyl-10-pentyl-15-(4-methoxyphenyl)-20-phenylporphyrin **176** was different compared to **193** as one phenyl ring is present (one of the aryl ring has no substitution at *para* position in this case). Surprisingly, **176**

exhibits only one singlet at lower field (9.58 ppm) for the two magnetically equivalent protons H7/H8 as they are flanked by two meso alkyl residues in 5- and 10- positions.

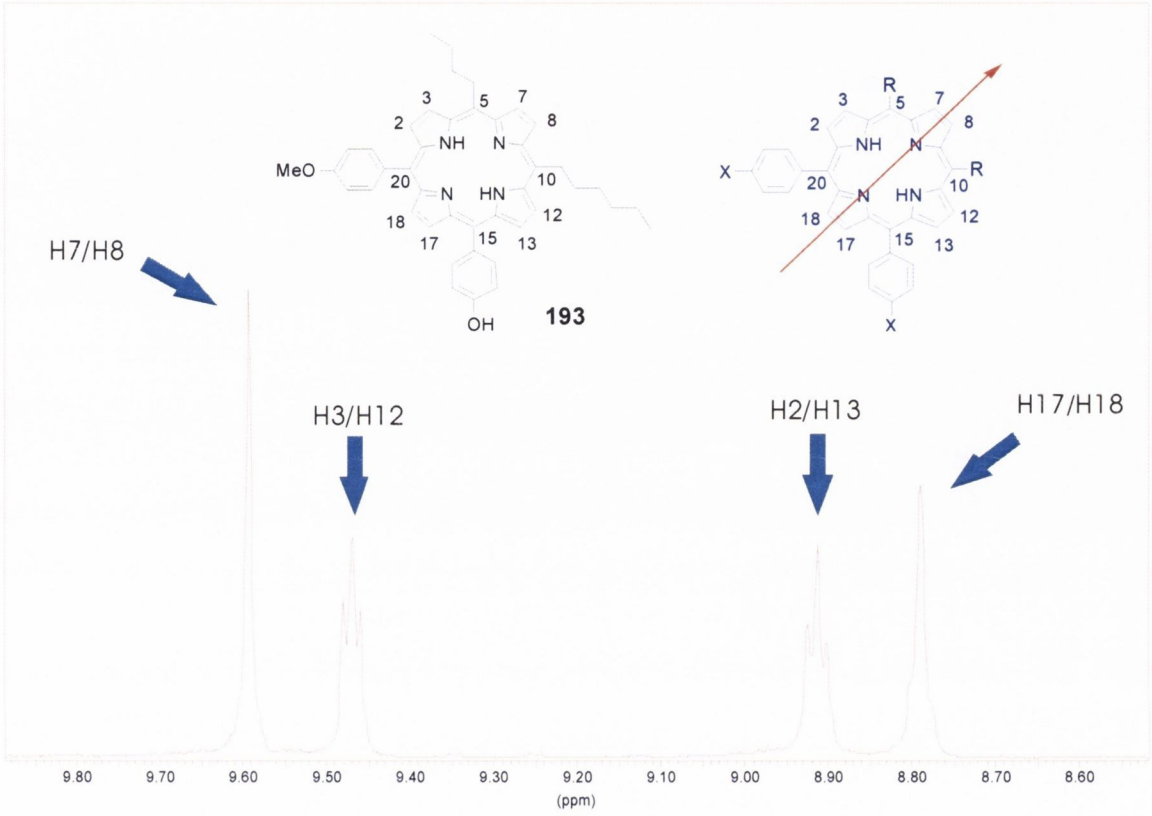


Figure 4.4. ^{1}H NMR spectrum of the β-pyrrole of **193** in $CDCl_3$.

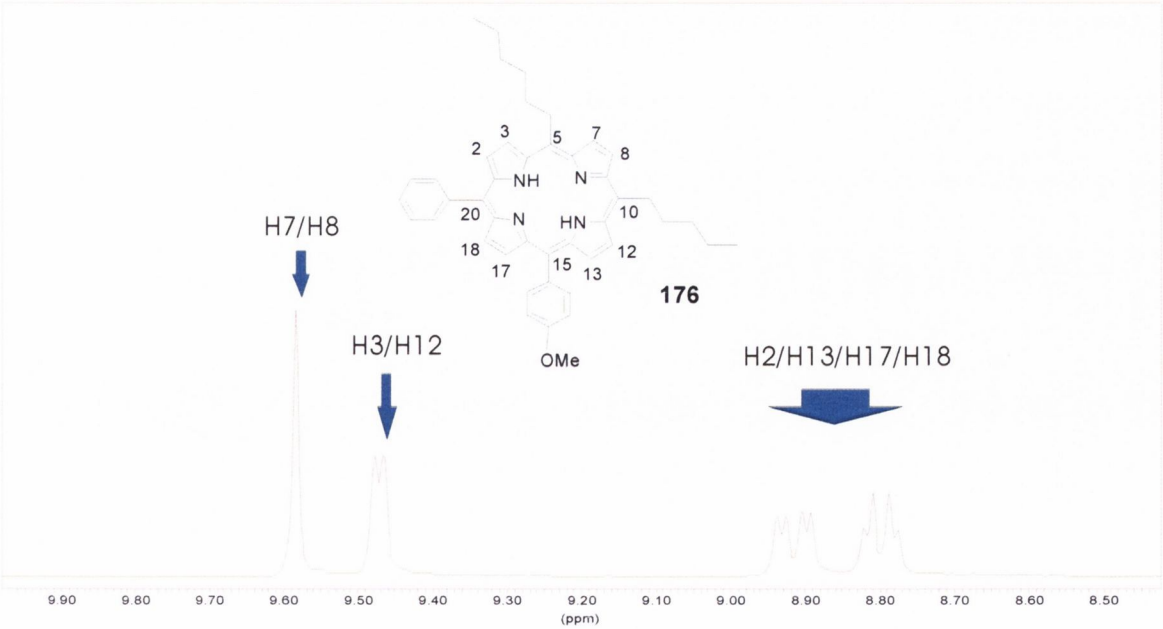


Figure 4.5. ^{1}H NMR spectrum of the β-pyrrole of **176** in $CDCl_3$.

As H2/H13/H17/H18 are in proximity to two aryl residues, they appear upfield at 8.78-8.92 ppm compared to H3/H7/H8/H12 due to the ring current effect of the phenyl rings (Figure 4.5).[121]

Further interesting information was obtained after examination of the β-pyrrole protons in ABCD-porphyrins containing three different aryl residues and one alkyl residue; namely, 5-(3,5-dimethoxyphenyl)-10-(4-hydroxyphenyl)-15-hexyl-20-phenylporphyrin **195**. The main difference between **195** and the two previous ABCD-porphyrins **176** and **193** is the replacement of one alkyl residue by an aryl residue. It is evident from Figure 4.6 that two protons (H13/H17) appear separately at the low-field (9.50 ppm) at the end of the β-pyrrole ^{1}H NMR spectrum as they are closest to the hexyl group while the remainder of the β-protons (H2/H3/H7/H8/H12/H18) closest to the three aryl residues appear at the start of the β-pyrrole ^{1}H NMR spectrum at 8.79-8.97 ppm. As H3/H7 are in proximity to the highly substituted aryl residue (3,5-dimethoxyphenyl group) as well as being flanked by the other two aryl residues, they appear separately at the high-field shift at 8.79 ppm (Figure 4.6).

Clearly, the chemical shift and splitting of the β-protons depend on the arrangement of the substituents at the meso positions and on the systematic replacement of phenyl/*para*-substituted phenyl or alkyl/aryl substituents and are a consequences of the numbers of meso-substituents.[59,117]

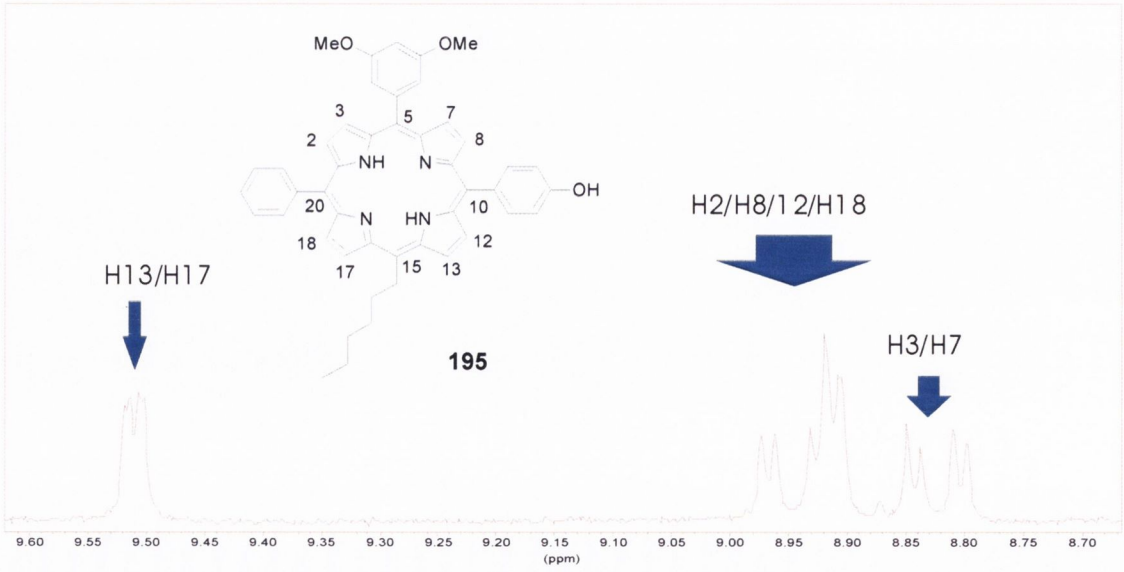


Figure 4.6. ^{1}H NMR spectrum of the β-pyrrole of **195** in $CDCl_3$.

The chemical shift of the N—H protons show a clear linear downfield trend as the number of meso-substituents is increased (AB- to ABC- to ABCD-type). Figure 4.7 indicate the change of N—H proton signals from —3.00 (**171**, AB-type) to —2.92 (**185**, ABC-type) to —2.74, —2.66, —2.64 ppm (**195**, **193** and **176**, respectively, ABCD-types). Although **193**, **176** and **195** are ABCD-porphyrins, the N—H proton signals for **195** (with three aryl substituents) shows more of an upfield shift (—2.74 ppm) compared to the case of **193** and **176**. This suggests that the shielding effect of the macrocyclic ring current on the N—H protons increases proportionately with the number of aryl substituents (Figue 4.7).[59]

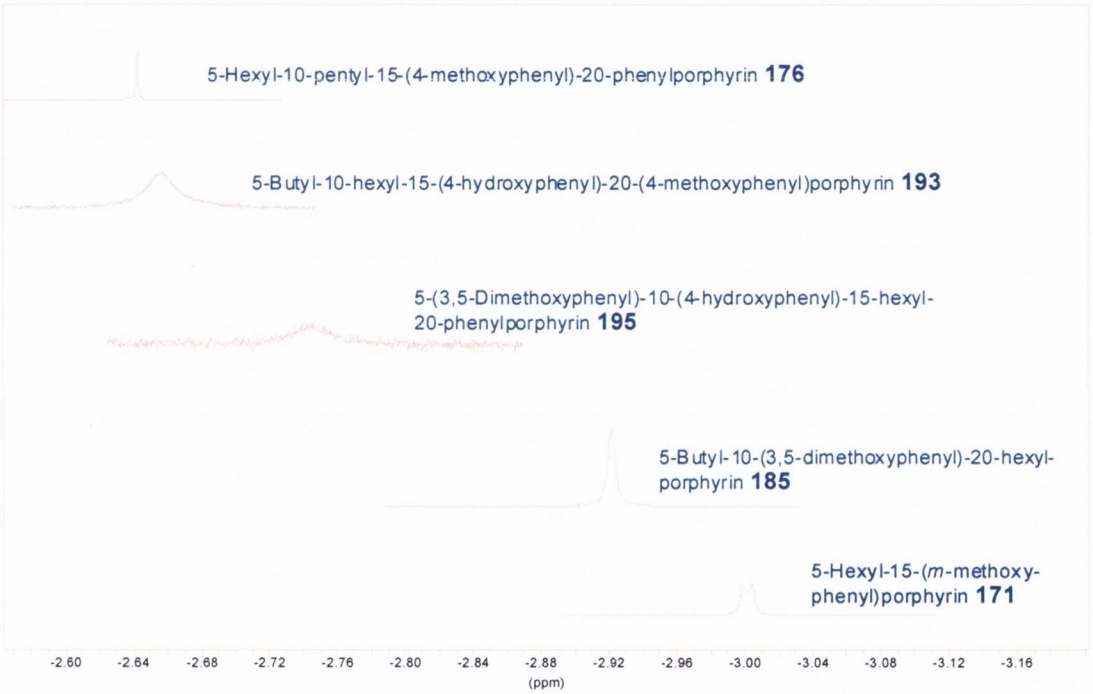


Figure 4.7. ^{1}H NMR spectrum of the N—H hydrogens of porphyrins **171**, **185**, **195**, **193** and **176** in $CDCl_3$.

4.1 Concluding remarks

This chapter focused on the synthesis of porphyrins bearing four different meso substituents (ABCD-porphyrins).

The first strategy described the one-pot synthesis of free base ABCD-porphyrins. This method allows the synthesis of various meso-functionalized free base porphyrins *via* combination of organolithium and iodides reagents in a one-pot reaction.The reactions proved to be controlled by optimization of the reaction conditions.

In addition, new ABC-porphyrins were formed during attempts to synthesize ABCD-porphyrins. These, ABC-porphyrins still have a free meso position which can be used for further functionalizations using organolithium reagents to form another series of target ABCD-porphyrins suitable for medicinal and biological studies. The mechanistic proposal for these reactions presumes that the phlorin-type intermediate is the key intermediate of the formation of ABC-porphyrins.

Unexpectedly, an efficient functionalization of the 5,15-disubstituted AB-porphyrins was done by using *p*-aminophenyllithium accompanied by dialkylation of the intermediary dilithiated amino group *via* propyl iodide to form the novel free base ABC-porphyrin **190** by introducing three substituents in one-pot reaction.

The second strategy focused on the preparation of ABCD-type porphyrins *via* two-step synthesis through functionalization of the respective AB-porphyrins by S_NAr reactions with organolithium reagents. Scheme 4.8 and 4.9 outlined two important examples of the synthesis of ABCD-porphyrins in acceptable yields carrying both precursors for *p*-hydroxyphenyl group and various alkyl chains which are suitable for biological studies.

Chapter 5

Synthesis of new chlorins, phlorins and porphodimethenes using organolithium reagents

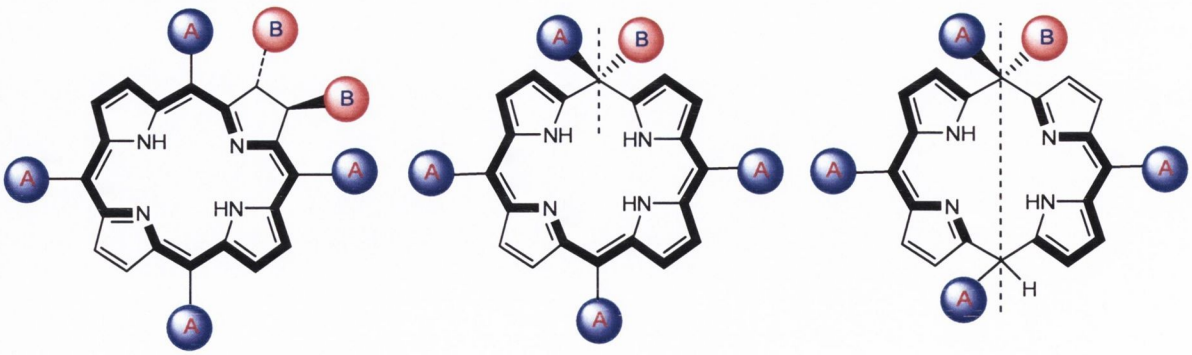
5.1 Introduction

The development of new efficient photosensitizers for use in photodynamic therapy (PDT) has received much attention in the past decade. As mentioned previously, most photosensitizers used in PDT are substituted derivatives of porphyrin, chlorin, and bacteriochlorin. Therefore, the search for new photosensitizers points to improve photophysical properties like absorption in the red region and this can be achieved by modification of the β-positions of the porphyrin ring especially *via* addition reactions at the "exocyclic" double bonds to yield chlorins.[145-147]

As we clarified in Chapter 1, porphyrins are aromatic macrocycles containing a total of 22 conjugated π electrons, 18 of which are incorporated into the delocalization pathway. Thus, one or two of the peripheral double bonds of porphyrins can undergo addition reactions to form chlorins or bacteriochlorins, without substantial loss of the macrocycle aromaticity.

The steric and electronic effects of porphyrin substituents are often a determinant of macrocycle reactivity towards addition reactions. Bulky porphyrin substituents shield reaction sites at the adjacent unsubstituted peripheral positions.

The relief of macrocyclic steric strain in overcrowded porphyrins bearing substituents at a meso positions is achieved by formation of the corresponding chlorin **196**, phlorin **197**, or porphodimethene **198** (Figure 5.1), which place the bulky substituents out of the macrocyclic plane. Although in **197** and **198** the saturated meso positions cause an interruption in the macrocyclic conjugation, the relative energies of these systems compared with the sterically overcrowded porphyrins are often very close.



196 **197** **198**

Figure 5.1. Structural formulas of chlorin, phlorin and porphodimethene **196**, **197** and **198**.

The goal of the present study was the synthesis of new chlorins, in which one β,β`-bond of a porphyrin is formally reduced, because of the importance of chlorins in photosynthesis and their utilization as photosensitizers in photodynamic therapy (PDT). In addition, modification of the electronic structure of β-positions of the porphyrin ring by conversion to chlorin is important in improvement of photophysical properties like absorption in the red region, singlet oxygen quantum yield and localization of the photosensitizer within the tumour cell.

5.2 Results and discussion

We aim to improve a general method to generate chlorins from porphyrins and modify the β-position by changing the electronic structure *via* addition reactions.

It is clear from Figure 5.1 that the starting materials used are meso-tetrasubstituted (A_4-type) symmetric porphyrin. As these porphyrins have free β- and occupied meso positions, some directing effect towards either the β-positions forming chlorins or further attack at the meso position forming phlorins or porphodimethenes was expected.[116,148]

We have used organolithium reagents as highly reactive and versatile reagents to achieve the modification of the β-position(s) to form chlorin. Although many methods are available for chemical transformation involving the β-position(s) of A_4 porphyrins, our recent methods *via* organolithium reagents are more simple and facile and perform the generation of chlorins *via* straightforward method.

The nature of the substituents on porphyrins (the steric and electronic effects) can influence the reactivity of the macrocycle. Although the chemical reactivity of porphyrins is often determined by electronic and steric effects, there are various other factors that can also influence the reactivity pattern of these macrocycles, like the steric demand of the organolithium reagent used, the solvent and the reaction temperature. Indeed, these factors together can affect the nucleophilic attack of the organolithium reagent on the meso or β-positions.

^{1}H NMR spectra of the N—H protons can be used for detection if the formed product is chlorin or porphodimethene derivatives. The N—H protons in case of chlorins are more downfield shift than porphyrins but still < 0 ppm. The N—H protons of chlorins appear at −1 to −2 ppm while the N—H protons of porphyrins appear at −2 to −4 ppm according to the degree of substitution at the meso positions. On the other hand, the N—H protons of phlorins and

porphodimethenes appear at low field from 10 to 13 ppm and in some cases splitted into two broad bands. It is clear that the huge shift of the N—H protons from the negative values to more than 10 ppm is due to lacking the aromatic conjugated system in case of phlorins and porphodimethenes and the N—H protons become inside the deshielding area of the macrocycle.[148]

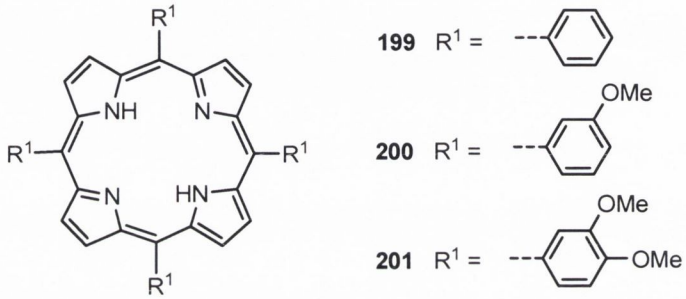
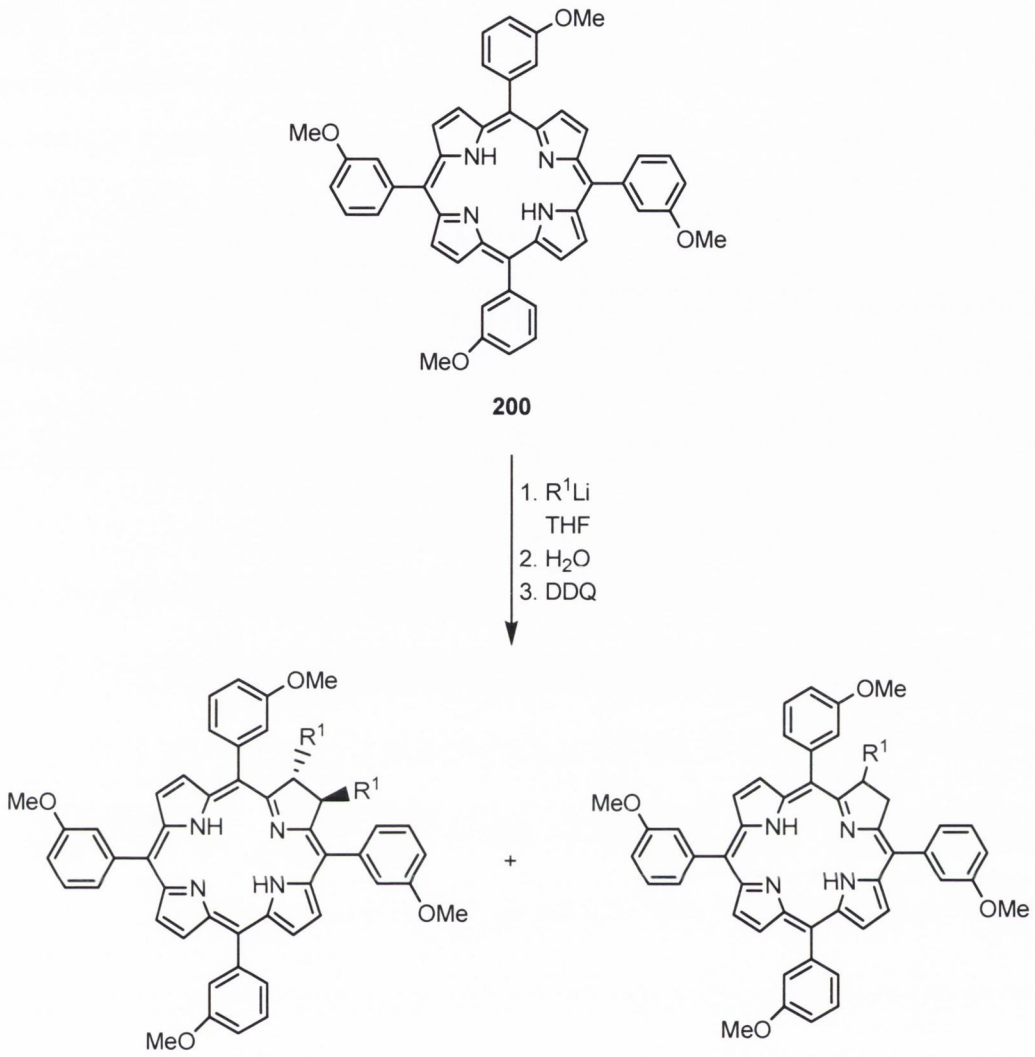


Figure 5.2. Different A_4-type porphyrins.

Callot had shown that 5,10,15,20-tetraphenylporphyrin H_2(TPP) **199** (Figure 5.2) reacts with *n*-BuLi in 18 % yield to give a phlorin *via* attack at the meso position. In addition, he observed the formation of a chlorin in 7 % yield as the product of *n*-BuLi addition to a C_β-C_β double bond. [116,148]

Senge *et.al.* found that Zn^{II}(TPP) reacts with *n*-BuLi in a similar manner. However, two chlorins, the mono- and dibutylated products were obtained in 6.5 and 18 % yields respectively.[58] Thus, for meso-aryl porphyrins both meso- and β attack of RLi are possible.

Since no general method exists in which attack on the meso or β-positions on an A_4-porphyrin is preferantially controlled, [15,30,149,150] we have investigated in this chapter the reactions of various RLi with different A_4-porphyrins **199-201** (Figure 5.2). Initially, we used 5,10,15,20-tetrakis(3-methoxyphenyl)porphyrin **200** as a starting material with methoxy group on the phenyl ring. These groups although having an electron-withdrawing inductive effect, is electron-donating by resonance and therefore tend to increase the nucleophilic character of the porphyrin macrocycles.



	R^1 =	
203	*n*-butyl	14 %
205	*n*-hexyl	20 %
207	*sec*-butyl	18 %

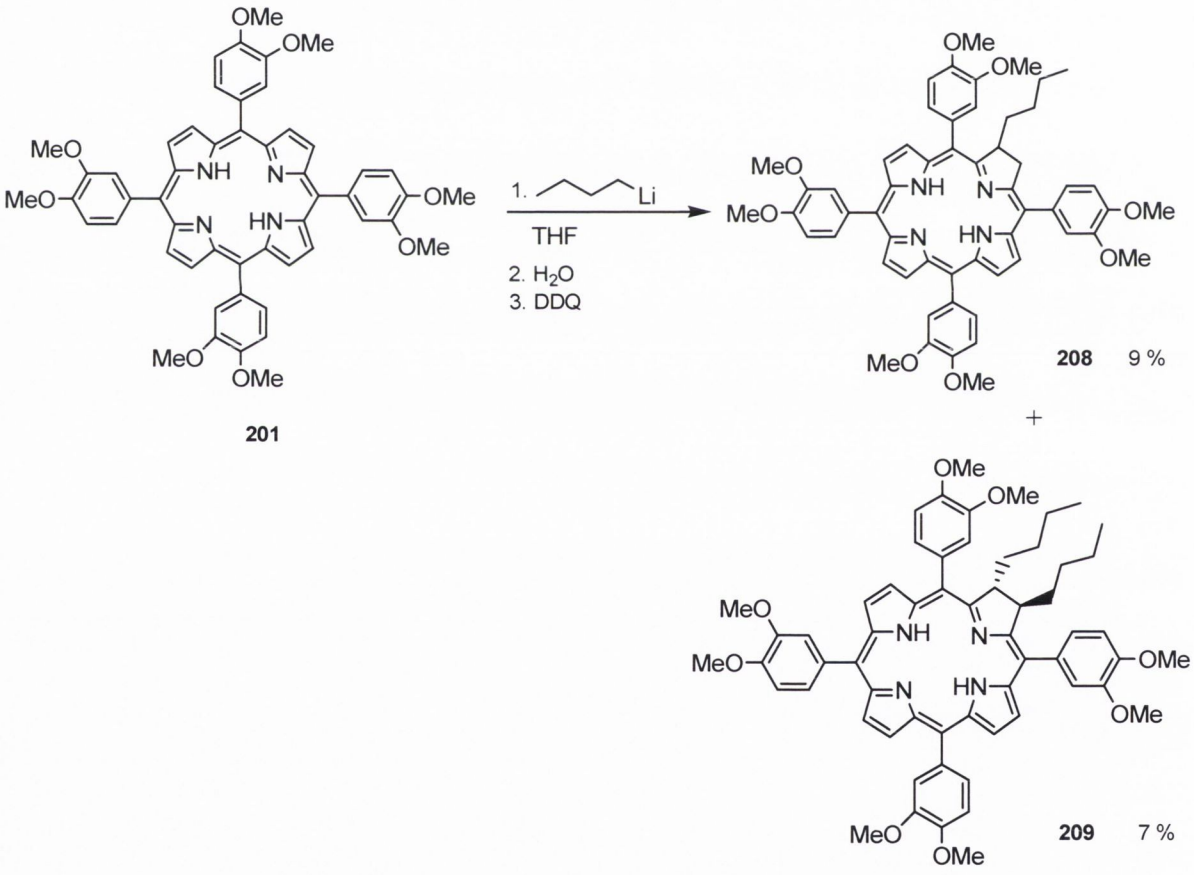
	R^1 =	
202	*n*-butyl	17 %
204	*n*-hexyl	22 %
206	*sec*-butyl	25 %

Scheme 5.1. Reaction of **200** with organolithium reagents.

5,10,15,20-Tetrakis(3-methoxyphenyl)porphyrin **200** was reacted with alkyllithium reagents (*n*-butyl, *n*-hexyl, and *sec*-butyllithium reagents) in dry THF at −80 °C followed by hydrolysis with water and oxidation with DDQ. The reaction yielded two chlorins: the

monoalkylated products **202**, **204** and **206** and the dialkylated products **203**, **205** and **207** in yields 10 — 25 % with the starting materials (Scheme 5.1). The UV/Vis spectra of **202-207** are typical for chlorins as well as the ^{1}H NMR signals which clearly show the protons attached to the sp^3-carbon atoms C-2 and C-3. In addition, the ^{1}H NMR data are compatible with the expected chlorin structures: All signals of pyrrolic protons are present in the δ = 8.5 — 9.7 range and the N-H signals are found in the range —1 to —2 ppm.

In the same manner, 5,10,15,20-tetrakis(3,4-dimethoxyphenyl)porphyrin **201** was reacted with *n*-butyllithium reagent in dry THF at —80 °C followed by hydrolysis with water and oxidation with DDQ forming two chlorins; the monobutylated products **208** and the dibutylated products **209** in 9 and 7 % yield, respectively (Scheme 5.2).

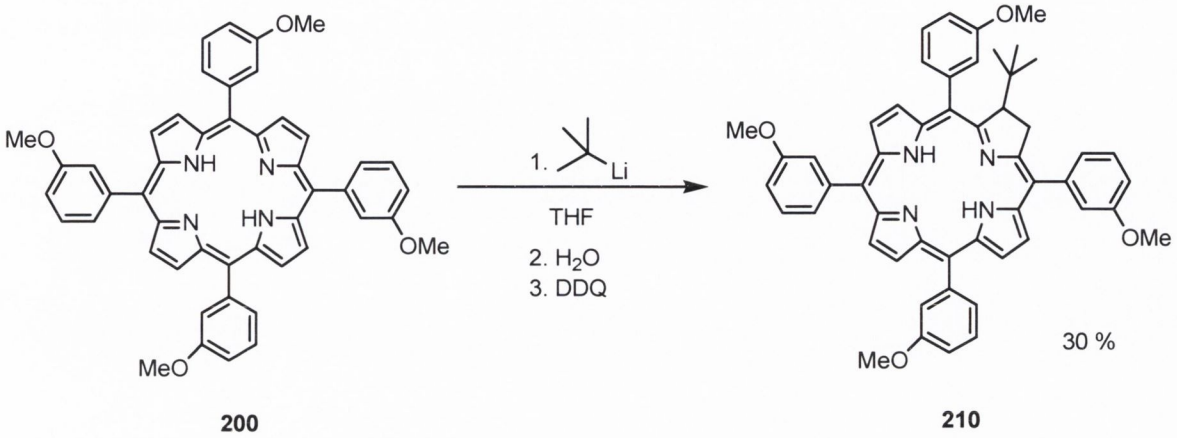


201

Scheme 5.2. Reaction of **201** with *n*-butyllithium reagent.

Interestingly, *t*-butyllithium showed a different reactivity behaviour towards the free base 5,10,15,20-tetrakis(3-methoxyphenyl)porphyrin **200.** Only the monoalkylated product **210** was formed as a sole reaction product under the same reaction conditions like with alkyllithium

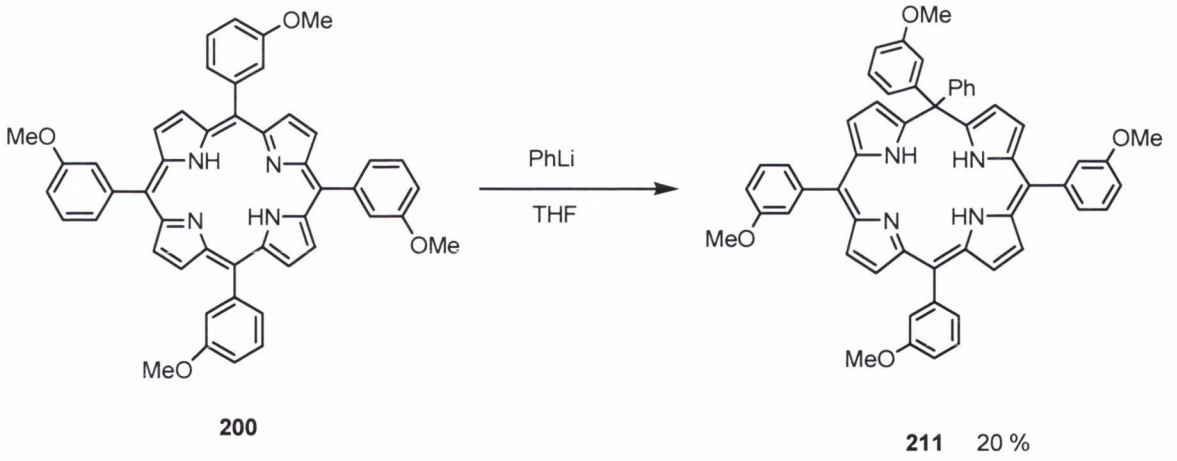
reagents (*n*-butyl, *n*-hexyl, and *sec*-butyllithium) due to the steric hinderance of the *t*-butyl group (Scheme 5.3).



200 **210**

Scheme 5.3. Reaction of **200** with *t*-butyllithium reagent.

On the other hand, the free base tetrakis(3-methoxyphenyl)porphyrin **200** reacted with phenyllithium reagent *via* attack at the meso position forming the phlorin **211** in 20 % yield. No chlorins were formed in this case (Scheme 5.4).

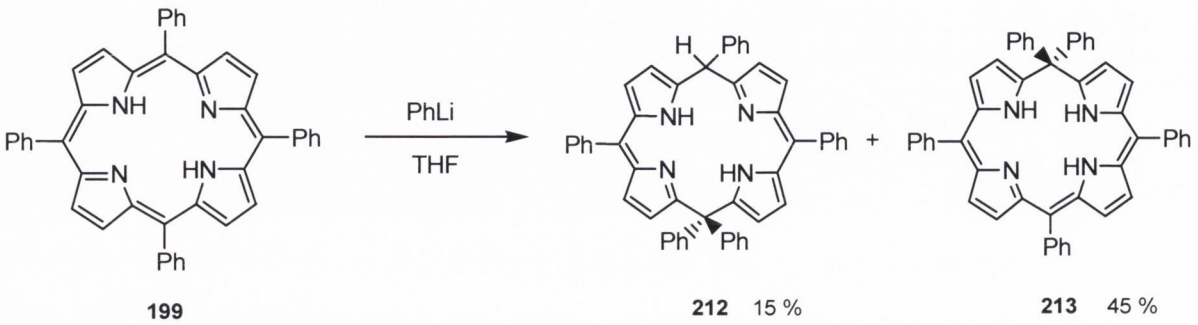


200 **211** 20 %

Scheme 5.4. Reaction of **200** with phenyllithium.

Indeed, the previous reaction led us to react 5,10,15,20-tetraphenylporphyrin H_2(TPP) **199** with phenyllithium. Interestingly, two products were found, the porphodimethene **212** in 15 % yield and phlorin **213** in 45 % yield. ^{1}H NMR data of the β-pyrrole and N—H protons are compatible with the structures **212** and **213** and confirm the loss of aromaticity for the porphyrin ring (Scheme 5.5).

The formation of **212** and **213** via further attack at the 5-meso-position indicate the formation of both phlorin and porphodimethene intermediates and an equilibrium between the two intermediates exists. The formation of **212** and **213** after the hydrolysis and the oxidation steps indicates that the porphodimetheme **212** is stable and resist oxidation with DDQ.[57]



199 **212** 15 % **213** 45 %

Scheme 5.5. Reaction of **199** with phenyllithium.

5.2.1 ^{1}H-NMR spectra of β-protons of A_4-porphyrins, mono- and dialkylated chlorins

Anlogous to the ^{1}H NMR spectroscopy of the β-pyrrole protons of various unsymmetrically substituted porphyrins, a comparative analysis of the pattern of β-pyrrole protons of A_4-porphyrin, mono- and dialkylated chlorins was performed. As expected, as A_4-type porphyrin has four symmetry axes, two of them passing through the meso carbons and the other two bisecting the pyrrole units, β-pyrrole protons (H2/H3/H7/H8/H12/H13/H17/H18), being magnetically equivalent, give a singlet at 8.92 ppm (Figure 5.3). Although the singlet peak formed in the case of A_4 porphyrins is identical with that formed in the case of porphine **1** (Figure 2.4, Chapter 2), the chemical shift shows a clear moving to higher fields compared to the value recorded for porphine **1** (9.56 ppm).[59,151]

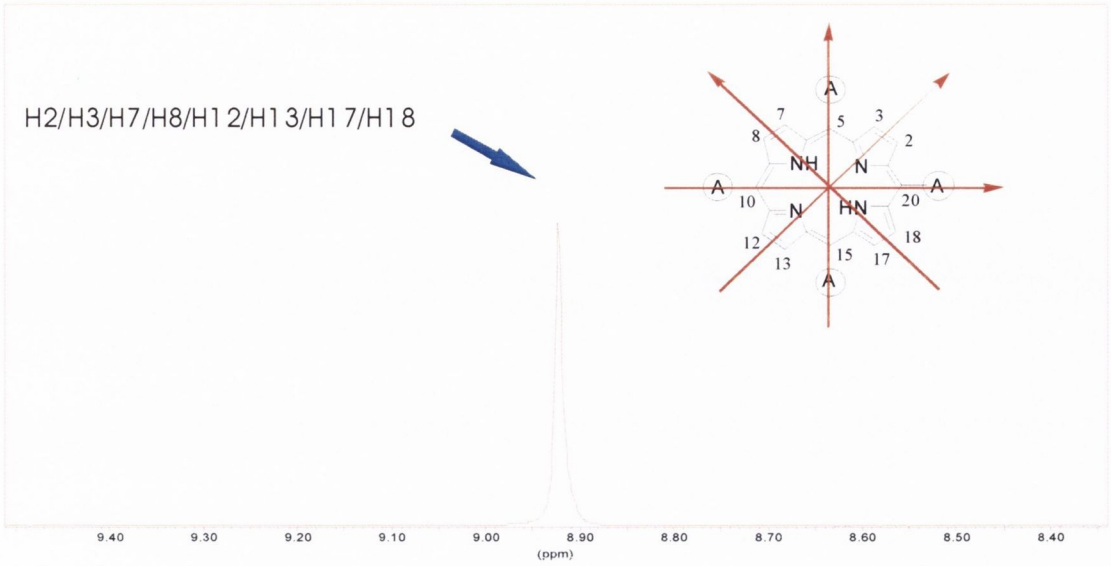


Figure 5.3. ^{1}H NMR spectra of the β-pyrrole of A_4-type porphyrin.

^{1}H NMR data of the β-pyrrole protons of 7,8-dialkylated porphyrins, examplified by *trans*-7,8-dibutyl-5,10,15,20-tetrakis(3,4-dimethoxyphenyl)chlorin **209**, shows a singlet for H17/H18 at 8.51 ppm. H17 and H18 are magnetically equivalent due to the presence of a symmetry axis bisecting the two pyrroles bearing H17/H18 and the two butyl groups (Figure 5.4).[117,120] **209** also exhibits two sets of two magnetically equivalent nuclei as multiplets at 8.28 ppm for H3/H12 (near to the two butyl groups) and at 8.67 ppm for H2/H13 (Figure 5.4).

In case of 7-Butyl-5,10,15,20-tetrakis(3,4-dimethoxyphenyl)chlorin **208** with one butyl group, H3 and H12 become non-equivalent due to the effect of the butyl group and give two doublets at 8.25 and 8.28 ppm, respectively (Figure 5.5). Surprisingly, the rest of β-protons in **208** appear identical to **209** with the same chemical shift. H17/H18 appears as a singlet at 8.51 ppm and H2/H13 appear as a multiplet at 8.67 ppm (Figure 5.5).

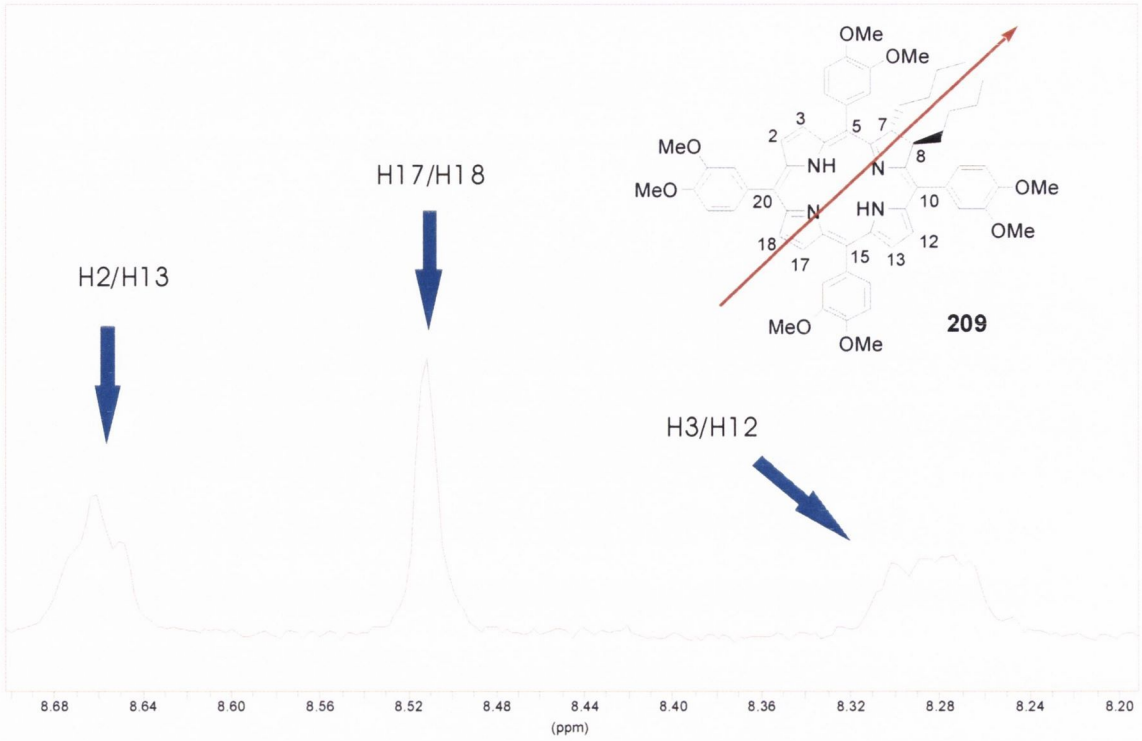


Figure 5.4. ^{1}H NMR spectra of the β-pyrrole of **209**.

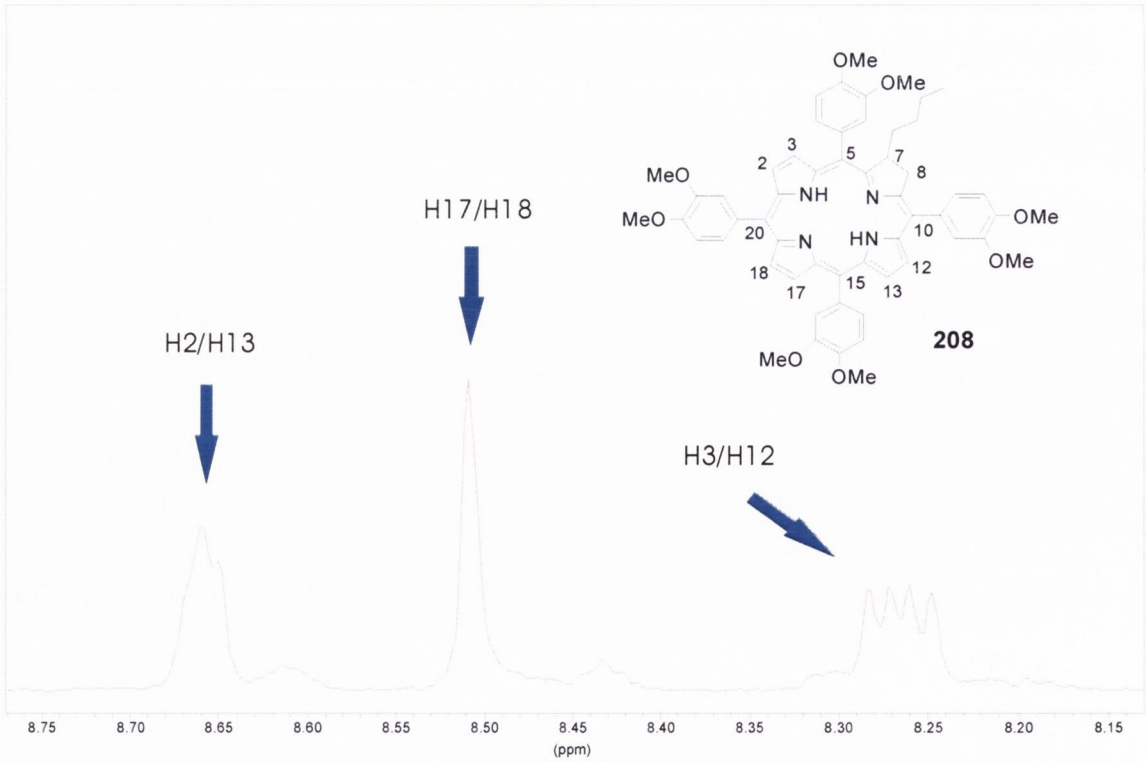


Figure 5.5. ^{1}H NMR spectra of the β-pyrrole of **208**.

5.3. Conclusions

The present results clearly show that A_4-porphyrins react readily with organolithium reagents in a simple, facile and straightforward manner and can be used for the generation of chlorins, porphodimethenes and/or phlorins.

The nature of the substituents on the porphyrins (the steric and electronic effects) influence the reactivity of the macrocycle. However, there are other factors that can also influence the reactivity pattern of these macrocycles, such as the steric demand of the organolithium reagent used. Indeed, these factors affect the nucleophilic attack of the organolithium reagent on meso or β-positions.

Chapter 6

Experimental

6.1 General methods

All chemicals used were of analytical grade and were purchased from Aldrich Co. unless stated otherwise. Dichloromethane was dried over phosphorus pentoxide followed by distillation; THF was dried over sodium followed by distillation. All condensation reactions were performed under an argon atmosphere with the reaction flask shielded from ambient light. Reactions with organolithium reagents were performed using standard Schlenk techniques and glassware under an argon atmosphere. Melting points were measured on a Reichert Thermovar apparatus and are uncorrected. Silica gel 60 (Merck or Machery & Nagel) was used for column chromatography. Analytical thin-layer chromatography (TLC) was carried out using Merck silica gel 60 plates (precoated sheets, 0.2 mm thick, with and without fluorescence indicator F_{254}). Proton NMR spectra were recorded at a frequency of 250 (AC 250), 300 or 400 MHz (Bruker, Avance DPX 400), ^{13}C NMR spectra were recorded at a frequency of 60 or 100 MHz. All chemical shifts are given in ppm, listed on the δ-scale and are referenced to $SiMe_4$ (TMS) signal as internal standard. **Figure 6.1** illustrate the atom numbering and assignment used in the description of the NMR data.

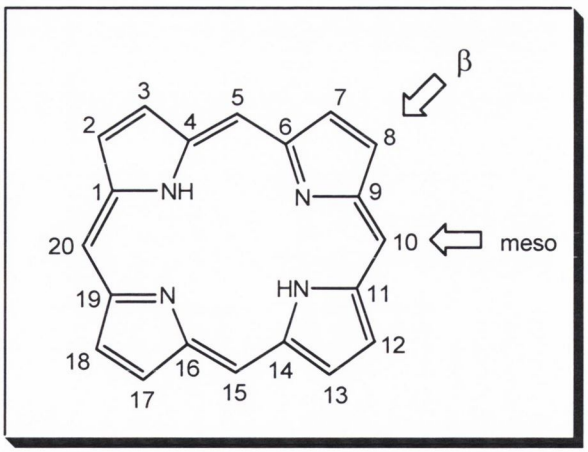


Figure 6.1 Porphyrin numbering used in the NMR assignments.

Electronic absorption spectra were recorded on a Specord S10 (Carl Zeiss) spectrophotometer using dichloromethane as solvent. Mass spectra were recorded using a Varian MAT 711 or MAT 112 S mass spectrometer using the EI technique with a direct insertion probe and an

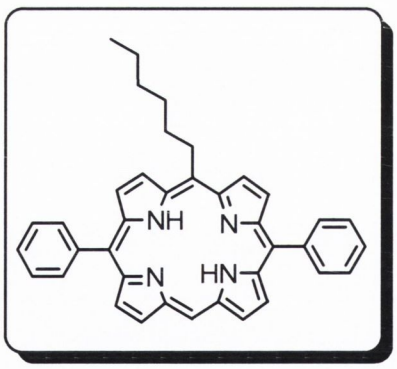
excitation energy of 80 eV. FAB spectra were recorded with CH-5 DF instrument from Varian. In addition, HRMS were recorded using Micromass TOF fitted with an EI probe. All yields are given with respect to the porphyrin used in the reactions.

6.2 Starting materials

Dipyrromethane **31**,[78,79] 5,15-diphenylporphyrin **42**,[48,29] 5,15-bis(*m*-methoxyphenyl)porphyrin **107**,[125] 5-(*p*-aminophenyl)-10,20-diphenylporphyrin **127**,[62] 5,10,15,20-tetraphenylporphyrin [H2(TPP)] **199**,[30] 5,10,15,20-tetrakis(*m*-methoxyphenyl)porphyrin **200**,[30] and 5,10,15,20-tetrakis(3,4-dimethoxyphenyl)porphyrin **201**[30] were prepared according to literature procedures.

6.3 Syntheses

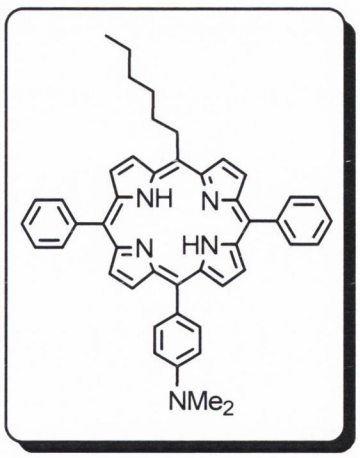
5-Hexyl-10,20-diphenylporphyrin 101



n-Hexyllithium (1.7 mL of a 2.5 M solution in hexane, 3.4 mmol) was added under an argon atmosphere to a 100 mL Schlenk flask charged with a solution of 5,15-diphenylporphyrin **42** (220 mg, 0.47 mmol) in 40 mL of dry THF at −80 °C. The color of the mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 5 h at R.T. (TLC control). Subsequently, a mixture of 2 mL of water in 3 mL of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equiv of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. The mixture was filtered through silica gel (Merck) and the organic solvent was removed under

vacuum or washed with enough *n*-hexan. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1:7, v/v) yielding the title compound (185 mg, 0.34 mmol, 71%) as purple crystals, mp > 300 °C; $R_f = 0.62$ (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = -2.95$ (s, 2H, N*H*), 0.92 (t, 3H, $J = 7.2$ Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.38 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.83 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.52 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 5.02 (t, 2H, $J = 8.1$ Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.78 (m, 6H, *o,p*-Ph-H), 8.23 (m, 2H, m-Ph-H), 8.26 (m, 2H, m-Ph-H), 8.91 (m, 4H, β -pyrrole-H), 9.24 (d, 2H, $J = 5.0$ Hz, - β pyrrole-H), 9.59 (d, 2H, $J =$ 5.0 Hz, β-pyrrole-H), 10.18 ppm(s, 1H, meso-H); ^{13}C NMR (300 MHz, $CDCl_3$): $\delta = 14.54$ (5^{6}-C), 23.13 (5^{5}-C), 28.16 (5^{4}-C), 30.11 (5^{3}-C), 32.33 (5^{2}-C), 39.45 (5^{1}-C), 119.45, 121.64, 127.14, 128.07, 135.03, 142.49 ppm; UV/vis (CH_2Cl_2): λ_{max} (lg ε) = 412 (5.02), 510 (3.69), 544 (3.23), 583.59 (3.28), 655 nm (3.41); MS (EI, 80 eV): *m/z* (%): 546 (90) [M^+], 475 (100) [M^+-C_5H_{11}], 273 (26) [M^{++}]; HRMS [$C_{38}H_{34}N_4$]: calcd 546.2783, found 546.2759.

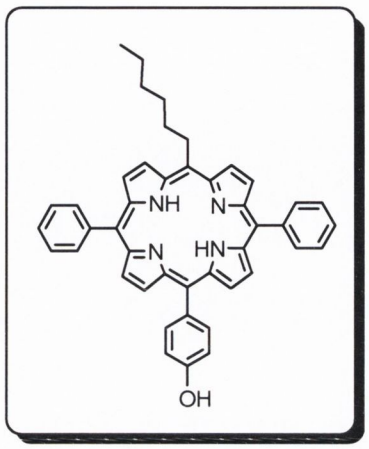
5-Hexyl-10,20-diphenyl-15-(*p*-dimethylaminophenyl)porphyrin 102



n-Butyllithium (1.2 ml of a 2.5 M solution in hexane, 3 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-(dimethylamino)bromobenzene (0.5 g, 2.5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for another 1 h at room temperature. The solution became yellow and opaque. To the vigorously stirred

mixture a solution of 5-hexyl-10,20-diphenylporphyrin **101** (100 mg, 0.18 mmol) in 40 ml of dry THF was added rapidly under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 3 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) and yielded the title compound (66 mg, 0.1 mmol, 54 %) as purple crystals, mp >300 °C; $R_f = 0.42$ (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.61 (s, 2H, N*H*), 0.92 (t, 3H, *J*=7.2, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.39 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.79 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.53 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.22 (s, 6H, $N(CH_3)_2$), 5.02 (t, 2H, *J* = 8.1, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.11 (d, 2H, *J* = 7.5, Ph-H), 7.76 (m, 6H, Ph-H), 8.06 (d, 2H, *J* = 7.5, Ph-H), 8.22 (m, 4H, Ph-H), 8.81 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 8.92 (m, 4H, β-pyrrole-H), 9.46 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.72 (15^6-C), 22.28 (15^5-C), 29.81 (15^4-C), 31.47 (15^3-C), 35.04 (15^2-C), 38.36 (15^1-C), 40.25(C_{NMe2}), 110.29, 118.85, 119.64, 126.12, 127.13, 128.33, 134.07, 135.25, 142.18, 149.45 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 419 (4.91), 517 (3.76), 564 (3.47), 595 (3.16), 653 nm (3.33); MS (EI, 80 eV): *m/z* (%): 665 (24) [M^+], 594 (25) [$M^+-C_5H_{11}$], 578 (10) [$M^+-C_5H_{12}-CH_3$], 333 (20) [M^{++}]; HRMS [$C_{46}H_{43}N_5$] : calcd 665.3518, found 665.3491.

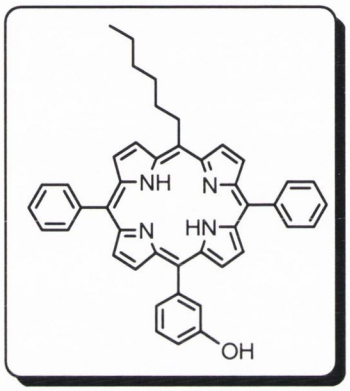
5-Hexyl-10,20-diphenyl-15-(*p*-hydroxyphenyl)porphyrin 103



n-Butyllithium (3 ml of a 2.5 M solution in hexane, 7.5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromophenol (0.87 g, 5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 18 h at room temperature. The solution slowly became white opaque. To the vigorously stirred mixture was added rapidly a solution of 5-hexyl-10,20-diphenylporphyrin **101** (100 mg, 0.18 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 3 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) and yielded the title compound (76 mg, 0.12 mmol, 65 %) as purple crystals, mp >300 °C; R_f= 0.33 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.94 (t, 3H, *J* = 7.2 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.36 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.51 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.81 (m,2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 2.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.99 (t, 2H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 6.46–6.49 (m, 3H, Ph-H), 6.99 (d, 2H, *J* = 7.5 Hz, Ph-H), 7.23–7.26 (m, 3H, Ph-H), 7.76 (m, 2H, Ph-H), 7.78 (s, 1H, O*H*), 7.98 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.20–8.23 (d, 2H, Ph-H), 8.82 (m, 4H, β-pyrrole-H), 8.95 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.48 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H);

^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.54 (5^6-C), 23.11 (5^5-C), 30.65 (5^4-C), 32.29 (5^3-C), 35.58 (5^2-C), 39.26 (5^1-C), 113.10, 117.45, 120.03, 121.16, 127.05, 128.10, 132.71, 134.95, 136.06, 142.72, 154.81 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 417 nm (4.96), 445 (4.51), 514 (4.28), 595 (4.14), 653 nm (4.15); MS (EI, 80 eV): *m/z* (%): 638 (18) [M^+], 567 (34) [$M^+-C_5H_{11}$], 319 (17) [M^{++}]; HRMS [$C_{44}H_{38}N_4O$]: calcd 638.3045, found 638.3027.

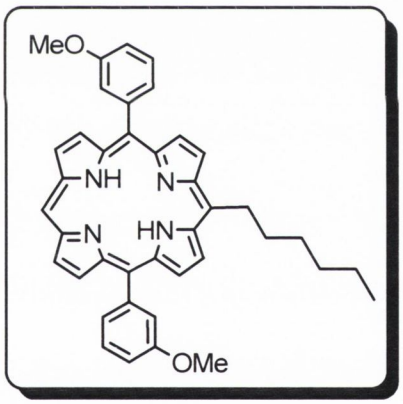
5-Hexyl-10,20-diphenyl-15-(*m*-hydroxyphenyl)porphyrin 106



n-Butyllithium (3 ml of a 2.5 M solution in hexane, 7.5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *m*-bromophenol (0.87 g, 5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 18 h at room temperature. The solution slowly became yellow opaque. To the vigorously stirred mixture was added rapidly a solution of 5-hexyl-10,20-diphenylporphyrin **101** (100 mg, 0.18 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 2 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) yielding the title compound (97 mg, 0.15 mmol, 83 %) as purple crystals, mp >300 °C; R_f = 0.55 (ethyl acetate/*n*-hexane, 1 : 3, v/v); ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.96 (t, 3H, J = 7.2 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.27 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.40 (m, 2H,

$CH_2CH_2CH_2CH_2CH_2CH_3$), 1.72 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.51 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.92 (t, 2H, J=8.1, $CH_2CH_2CH_2CH_2CH_2CH_3$), 6.41 (m, 1H, Ph-H), 6.69 (m, 1H, Ph-H), 6.95 (m, 1H, Ph-H), 7.45 (m, 1H, Ph-H), 7.67 (s, 1H, O*H*), 7.78 (m, 6H, Ph-H), 8.24 (m, 4H, Ph-H), 8.77 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 8.82 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 8.95 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 9.45 ppm (d, 2H, J = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.68 (5^6-C), 22.24 (5^5-C), 29.75 (5^4-C), 31.42 (5^3-C), 35.06 (5^2-C), 38.37 (5^1-C), 113.61, 118.16, 119.20, 120.49, 121.25, 122.13, 123.19, 126.18, 127.22, 130.08, 134.08, 141.90, 142.89, 153.26, 155.77 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε)=417 (4.97), 443 (4.22), 514 (3.76), 549 (3.55), 593 (3.48), 657 nm (3.56); MS (EI, 80 eV): *m/z* (%): 638 (16) [M^+], 567 (30) [$M^+-C_5H_{11}$], 319 (18) [M^{++}]; HRMS [$C_{44}H_{38}N_4O$]: calcd 638.3045, found 638.3025.

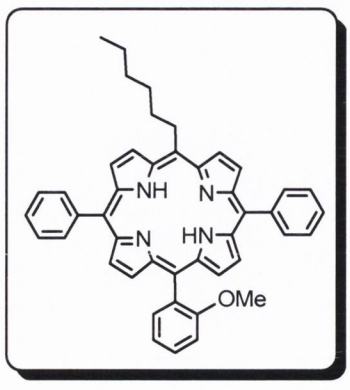
5,15-Bis(*m*-methoxyphenyl)-10-hexyl-porphyrin 108



5,15-Bis(3-methoxyphenyl)porphyrin **107** (160 mg, 0.31 mmol) was dried in vacuo in a septum-equipped Schlenk-flask for 2 h. THF (30 mL, abs.) was then added under argon. The porphyrin suspension was cooled to −70 °C. *n*-Hexyllithium (1.2 mL of a 2.5 M solution, 2.4 mmol) was added *via* a syringe through the septum. The cold bath was removed and the reaction mixture was stirred for 15 min at 20 °C. The solution changed its color from red to green-brown. Water (4 mL) was added and the solution was then stirred for 60 min. On addition of water the reaction mixture changed its color to dark-green. After this time, a solution of 10 equiv of DDQ in THF (0.06 M) was added, upon which the solution became dark red again. The reaction mixture was filtered through silica (3×50 cm), washing with

dichloromethane. The eluted porphyrin fractions were evaporated to dryness. The product was purified by column chromatography on silica (3×60 cm) using dichloromethane/n-hexane (3:1, v/v) as eluent. The porphyrin was again dissolved in as little dichloromethane as possible and then layered with a 2–3-fold excess of methanol. After 24 h, the precipitated solid was removed by suction filtration through a D3 frit and dried in vacuo to yield the title compound (120 mg, 0.2 mmol, 65%) of red-brown crystals: mp 226 °C; $R_f = 0.32$ (CH_2Cl_2/*n*-hexane, 3:1, v/v), 0.55 (CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = -3.03$ (s, 2H, N*H*), 0.91 (t, 3H, $J = 7$ Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.30 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.56 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.81 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.00 (s, 6H, OCH_3), 5.06 (t, 2H, J = 8 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.34 (m, 2H, Ph-H), 7.66 (m, 2H, Ph-H), 7.78–7.83 (m, 4H, Ph-H), 9.00 (m, 4H, β-pyrrole-*H*), 9.24 (d, $J = 5$ Hz, 2H, β-pyrrole-*H*), 9.52 (d, $J = 5$ Hz, 2H, β-pyrrole-*H*), 10.07 ppm (s, 1H, 20-meso-*H*); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 14.13, 22.72, 30.29, 31.92, 35.97, 39.04, 55.54, 103.99, 113.49, 118.76, 120.56, 121.24, 127.53, 127.72, 143.39, 158.04 ppm; UV/vis (CH_2Cl_2): λ_{max} (lg ε) = 303 (4.17), 372 (4.39), 393 (4.87), 413 (5.53), 478 (3.39), 509 (4.24), 543 (3.74), 584 (3.67), 639 nm (3.40); MS (EI, 80 eV, 310 °C), m/z (%): 606 (22) [M^+], 535 (9) [$M^+ - C_5H_{11}$], 303 (2) [M^{++}], 18 (100) [H_2O^+]; HRMS (EI) [$C_{40}H_{38}N_4O_2$]: calcd 606.29948, found 606.29907.

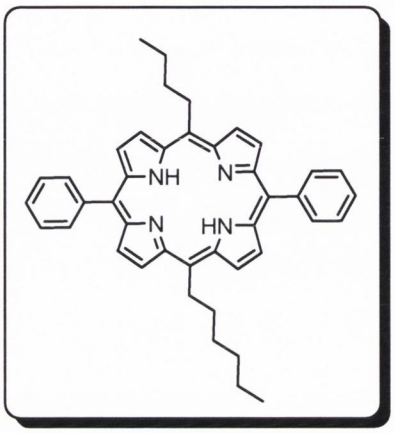
5-Hexyl-10,20-diphenyl-15-(*o*-methoxyphenyl)porphyrin 109



n-Butyllithium (2 ml of a 2.5 M solution in hexane, 5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *o*-bromoanisole (0.5 g, 2.7 mmol) in 10 ml of dry THF at −78 °C. After addition of *n*-butyllithium the cold bath was

removed and stirring was continued for 1 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5-hexyl-10,20-diphenylporphyrin **101** (50 mg, 0.09 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 12 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) yielded the title compound (24 mg, 0.04 mmol, 40 %) as purple crystals, mp >300 °C; R_f = 0.25 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.64 (s, 2H, N*H*), 0.96 (t, 3H, *J* = 7.2, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.28 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.85 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 2.56 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.59–3.78 (d, 3H, OCH_3), 5.04 (t, 2H, *J* = 8.1, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.01 (m, 1H, Ph-H), 7.37 (m, 2H, Ph-H), 7,79 (m, 6H, Ph-H), 8.01 (m, 1H, Ph-H), 8.22 (m, 4H, Ph-H), 8.76 (m, 4H, β-pyrrole-H), 8.92 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.49 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.14 (5^6-C), 22.71 (5^5-C), 30.23 (5^4-C), 31.90 (5^3-C), 35.58 (5^2-C), 38.81 (5^1-C), 55.66 (C_{OCH3}), 111.06, 115.18, 119.23, 120.74, 126.54, 127.55, 128.58, 130.88, 131.44, 135.56, 157.01, 159.42 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 416 (4.93), 443 (4.20), 514 (4.00), 565 (3.86), 594 (3.63), 649 nm (3.86); MS (EI, 80 eV): *m/z* (%): 652 (20) [M^+], 581 (35) [$M^+-C_5H_{11}$], 489 (18) [$M^+-C_5H_{11}-C_6H_5-CH_3$], 326 (15) [$M^{++}$]; HRMS [$C_{45}H_{40}N_4O$]: calcd 652.3202, found 652.3176.

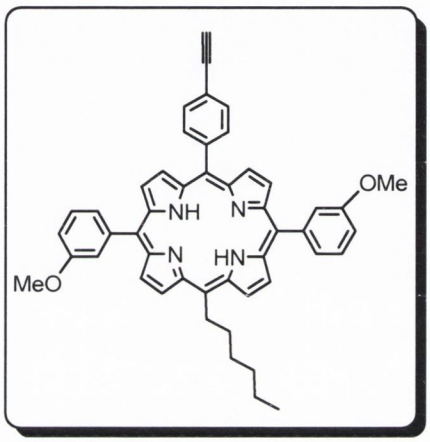
5-Butyl-10,20-diphenyl-15-hexylporphyrin 112



n-Butyllithium (2 ml of a 2.5 M solution in hexane, 5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-hexyl-10,20-diphenylporphyrin **101** (100 mg, 0.18 mmol) in 40 ml of dry THF at −80 °C. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 1 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with dichloromethane/*n*-hexane (2 : 1, v/v) and yielded the title compound (34 mg, 0.06 mmol, 31 %) as purple crystals, mp >300 °C; R_f = 0.77 (dichloromethane/*n*-hexane, 2 : 1, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.67 (s, 2H, N*H*), 0.94 (t, 3H, *J* = 7.2, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.13 (t, 3H, *J* = 7.2, $CH_2CH_2CH_2CH_3$), 1.27 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.52 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$),1.81 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.48 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.99 (t, 4H, *J* = 8.1, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.75 (m, 6H, Ph-H), 8.21 (m, 4H, Ph-H), 8.85 (m, 4H, β-pyrrole-H), 9.43 ppm (m, 4H, β-pyrrole-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.71 (15^6-C), 22.27 (15^5-C), 23.15 (5^4-C), 29.28 (5^3-C), 29.76 (15^4-C), 31.46 (15^3-C), 34.54 (5^2-C), 34.85 (15^2-C), 38.23 (15^1-C), 40.31 (5^1-C), 118.45, 119.36, 126.08, 127.14, 133.99, 142.26, 143.84, 146.70 ppm; UV/Vis

(CH_2Cl_2): λ_{max} (lg ε) = 417 (4.96), 438 (4.03), 515 (3.87), 550 (3.72), 592 (3.59), 651 nm (3.69); MS (EI, 80 eV) : *m/z* (%): 602 (60) [M^+], 559 (50) [$M^+-C_3H_7$], 531 (64) [$M^+-C_5H_{11}$], 488 (38) [$M^+-C_5H_{11}-C_3H_7$], 301 (26) [M^{++}]; HRMS [$C_{42}H_{42}N_4$] : calcd 602.3409, found 602.3383.

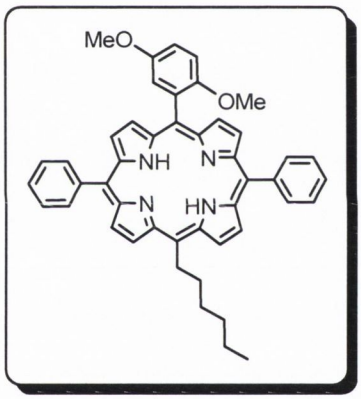
5-(*p*-Ethynylphenyl)-15-hexyl-10,20-bis(*m*-methoxyphenyl)porphyrin 113



n-Butyllithium (2 ml of a 2.5 M solution in *n*-hexane, 2.5 mmol) was added under an argon atmosphere to a 50 ml schlenk flask charged with a solution of *p*-bromophenylethyne (0. 45 g, 2.5 mmol) in 10 ml of dry diethyl ether at –70 °C. The reaction mixture was then warmed to – 40 °C and THF was added dropwise until the aryllithium was formed as a white-bright pink suspension. To this vigorously stirred mixture was added rapidly a solution of 5-hexyl-10,20-bis(*m*-methoxyphenyl)porphyrin **108** (50 mg, 0.082 mmol) in 30 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 2 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum or washed with enough *n*-hexane. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) and yielded the title compound (7 mg, 0.1 mmol, 12 %) as purple crystals, mp >300 °C; R_f = 0.49 (ethyl acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400

MHz, $CDCl_3$, TMS): δ = −2.72 (s, 2H, N*H*), 0.94 (t, *J* = 7.2, 3H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.28 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.56 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.84 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.61 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.34 (s, 1H, HC≡C), 4.02 (s, 6H, OCH_3), 5.05 (t, 2H, *J* = 8.1, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.38 (m, 2H, Ph-H), 7.69 (m, 2H, Ph-H), 7.82 (m, 4H, Ph-H), 7.89 (d, 2H, *J* = 7.6, Ph-H), 8.19 (d, 2H, *J* = 7.6, Ph-H), 8.78 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H2,8), 8.88 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H12,18), 8.98 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H3,7), 9.51 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H13,17); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 449 (5.10), 440 (3.97), 486 (3.32), 560 (2.15), 581 (3.05), 656 nm (4.29); HRMS [$C_{48}H_{42}N_4O_2$]: calcd 706.3308, found [M+1] 707.3365.

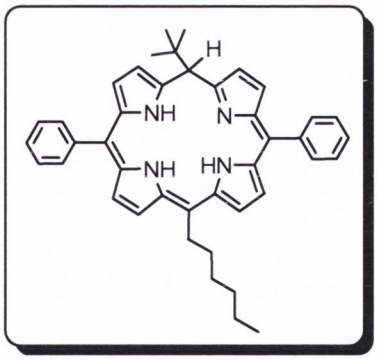
5-(2,5-Dimethoxyphenyl)-10,20diphenyl-15-hexylporphyrin 114



n-Butyllithium (2 ml of a 2.5 M solution in hexane, 5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 1-bromo-2,5-dimethoxybenzene (0.5 g, 2.4 mmol) in 10 ml of dry THF at −80 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 1 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5-hexyl-10,20-diphenylporphyrin **101** (50 mg, 0.09 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 5 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the

organic solvent was removed under vacuum or washed with enough *n*-hexane. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) and yielded the title compound (18 mg, 0.03 mmol, 29 %) as purple crystals, mp >300 °C; R_f = 0.22 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = − 2.66 (s, 2H, N*H*), 0.95 (t, 3H, *J* = 7.2, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.26 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.52 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.89 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.50–3.91 (m, 6H, OCH_3), 5.05 (t, 2H, *J* = 8.1, $CH_2CH_2CH_2CH_2CH_2CH_3$), 6.77 (m, 1H, Ph-H), 7.28 (m, 1H, Ph-H), 7,58 (m, 1H, Ph-H), 7.77 (m, 6H, Ph-H), 8.20 (m, 4H, Ph-H), 8.77 (m, 4H, β-pyrrole-H), 8.89 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.49 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.71 (15^6-C), 22.28 (15^5-C), 29.83 (15^4-C), 31.48 (15^3-C), 35.58 (15^2-C), 38.41 (15^1-C), 55.48, 56.27 ($2\times C_{OCH3}$), 111.60, 114.37, 117.30, 118.85, 120.96, 126.13, 127.15, 131.50, 134.00, 142.02, 151.99, 153.69 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 417 (4.97), 440 (3.97), 514 nm (3.83), 590 (3.57), 649 nm (3.61); MS (EI, 80 eV): *m/z* (%): 682 (20) [M^+], 611 (36) [$M^+-C_5H_{11}$], 341 (14) [M^{++}]; HRMS [$C_{46}H_{40}N_4O_2$]: calcd 682.3307, found 682.3275.

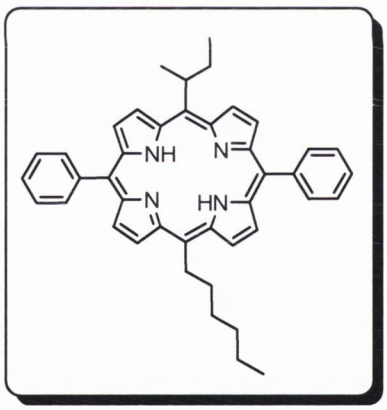
5-(*tert*-Butyl)-5,24-dihydro-10,20-diphenyl-15-hexylporphyrin 115



t-Butyllithium (1 ml of a 2.5 M solution in hexane, 2.5 mmol) was added under an argon atmosphere to a 50 ml schlenk flask charged with a solution of 5-hexyl-10,20-diphenylporphyrin **101** (50 mg, 0.09 mmol) in 30 ml of dry THF at −80 °C. The reaction mixture was stirred for 5 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10

equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 6, v/v) yielding the title compound (11 mg, 0.02 mmol, 20 %) as purple crystals, Mp = 227 °C; R_f = 0.43 (ethyl acetate/*n*-hexane, 1 : 1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 0.91 (t, 3H, *J* = 6, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.09 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.28 (s, 9H, $C(CH_3)_3$) 1.44 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.88 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.47 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.13 (t, 2H, *J* = 6, $CH_2CH_2CH_2CH_2CH_2CH_3$), 5.32 (s, 1H, 5-*H*), 6.04-6.47 (m, 4H, β-pyrrole-H), 6.51-6.85 (m, 4H, β-pyrrole-H), 7.14-7.59 (m, 6H, Ph-H), 7.87-7.96 (m, 4H, Ph-H), 10.39, 10.57 and 10.94 ppm (3 s, 3H, N*H*); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 376 (5.03), 435 (4.82), 578 (4.84), 656 (4.17) nm.

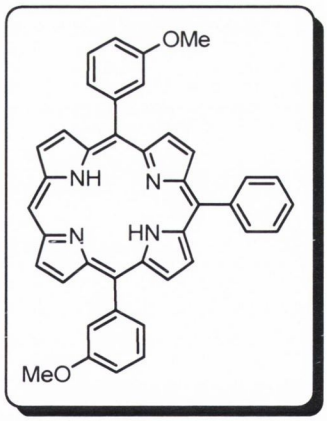
5-(*sec*-Butyl)-10,20-diphenyl-15-hexylporphyrin 117



sec-Butyllithium (1 ml of a 2.5 M solution in hexane, 2.5 mmol) was added under an argon atmosphere to a 50 ml Schlenk flask charged with a solution of 5-hexyl-10,20-diphenylporphyrin **101** (50 mg, 0.09 mmol) in 30 ml of dry THF at −80 °C. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 3 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic

solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 8, v/v) yielded the title compound (13 mg, 0.02 mmol, 25 %) as purple crystals, mp >300 °C; R_f = 0.75 (ethyl acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.56 (s, 2H, N*H*), 0.91 (t, 3H, *J* = 7.6, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.10-1.31 (m, 5H, $CH(CH_3)(CH_2CH_3)$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.44 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.88 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.42 (d, 3H, *J* = 7.4, $CH(CH_3)(CH_2CH_3)$), 2.52 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.75 (m, 2H, $CH(CH_3)(CH_2CH_3)$), 4.98 (t, 2H, *J* = 7.6, $CH_2CH_2CH_2CH_2CH_2CH_3$), 5.32 (m, 1H, $CH(CH_3)(CH_2CH_3)$), 7.77 (m, 6H, Ph-H), 8.22 (m, 4H, Ph-H), 8.86 (d, 4H, *J* = 5.0, β-pyrrole-H2,8,12,18), 9.43 (d, 2H, *J* = 5.0, β-pyrrole-H13,17), 9.57 ppm (d, 2H, *J* = 5.0, β-pyrrole-H3,7); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 441 (5.08), 486 (3.38), 514 (3.15), 581 (3.42), 656 nm (4.17); HRMS [$C_{42}H_{42}N_4$] : calcd 602.3409, found [M+1] 603.3487.

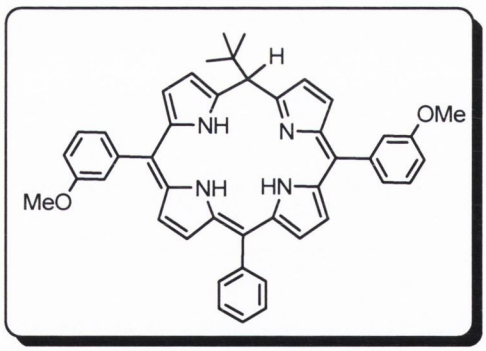
5,15-Bis(*m*-methoxyphenyl)-10-phenylporphyrin 121



Phenyllithium (2 ml of a 1.8 M solution in hexane, 0.06 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5,15-bis(*m*-methoxyphenyl)porphyrin **107** (200 mg, 0.38 mmol) in 40 ml of dry THF at −80 °C. The reaction mixture was stirred for 5 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel

(Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) yielding the title compound (163 mg, 0.27 mmol, 71 %) as purple crystals, mp >300 °C; R_f = 0.52 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.91 (s, 2H, N*H*), 4.02 (s, 6H, OCH_3), 7.41(m, 2H, Ph-H), 7.71−7.92 (m, 9H, Ph-H), 8.29 (m, 2H, Ph-H), 8.96 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.02 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.12 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.33 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 10.19 ppm (s, 1H, meso-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 55.06 ($2\times C_{OCH3}$), 104.34, 113.09, 118.94, 120.21, 126.12, 127.19, 130.96, 134.05, 142.11, 142.64, 157.66 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 413 nm (5.17), 441 (3.94), 508 (4.23), 541 (3.73), 582 (3.77), 637 nm (3.52); MS (EI, 80 eV): *m/z* (%): 598 (100) [M^+], 567 (10) [$M^+ - 2\times CH_3 - H$], 522 (8) [$M^+ - C_6H_4$], 491 (8) [$M^+ - 2\times CH_3 - C_6H_5$], 299 (86) [$M^{++}$]; HRMS [$C_{40}H_{30}N_4O_2$]: calcd 598.2368, found 598.2356.

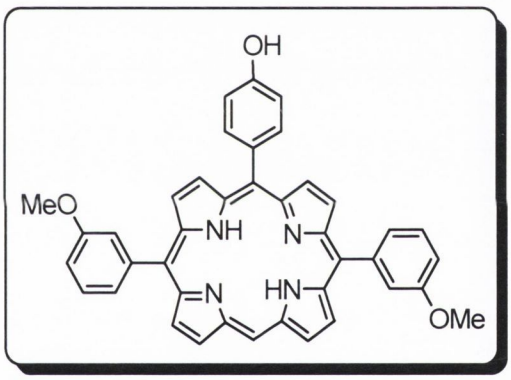
5-(*tert*-Butyl)-5,24-dihydro-10,20-bis(*m*-methoxyphenyl)-15-phenylporphyrin 122



t-Butyllithium (2 ml of a 1.8 M solution in hexane, 0.06 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 50 ml Schlenk flask charged with a solution of 5-Phenyl-10,20-bis(m-methoxyphenyl)porphyrin **121** (35 mg, 0.06 mmol) in 30 ml of dry THF. The mixture was heated to 50 °C and stirred for 30 min. Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.02 M) was added and the reaction mixture was stirred for

another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum or washed with enough *n*-hexane. Final purification was achieved by column chromatography and elution with ethyl acetate/n-hexane (1 : 8, v/v) yielded the title compound (11 mg, 0.016 mmol, 28 %) as purple crystals, mp = 226 °C; R_f = 0.47 (ethyl acetate/n-hexane, 1 : 1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 1.28 (s, 9H, C(CH_3)$_3$), 3.91 (s, 6H, OCH_3), 5.33 (s, 1H, 5-H), 6.01-6.43 (m, 4H, β-pyrrole-H), 6.53-6.66 (m, 4H, β-pyrrole-H), 6.87 (m, 2H, Ph-H), 7.06-7.15 (m, 4H, Ph-H), 7.37 (m, 3H, Ph-H), 7.51 (m, 4H, Ph-H), 9.88, 10.02 and 10.65 ppm (3 s, 3H, N*H*). UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 350 (4.85), 453 (4.69), 577 (5.11), 656 (4.15) nm.

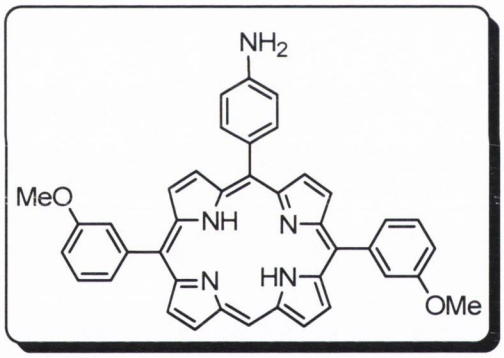
5-*p*-Hydroxyphenyl-10,20-bis(*m*-methoxyphenyl)porphyrin 124



n-Butyllithium (4 ml of a 2.5 M solution in hexane, 10 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromophenol (0.87g, 5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 18 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5,15-bis-(methoxyphenyl)porphyrin **107** (200 mg, 0.38 mmol) in 40 ml of dry THF under an argon atmosphere. Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum or washed with enough *n*-hexane. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 1, v/v) and yielded the title compound (182 mg, 0.29 mmol, 77 %) as

purple crystals, mp >300°C; R_f = 0.54 (ethyl acetate/*n*-hexane, 2 : 1, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 4.01 (s, 6H, OCH_3), 6.89 (d, 2H, Ph-H), 7.37 (d,2H, *J* = 7.5 Hz, Ph-H), 7.66 (t, 2H, Ph-H), 7.88 (m, 4H, Ph-H), 7.90 (s, 1H, O*H*), 7.97 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.91 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.00(d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.12 (d, 2H,*J* = 5.0 Hz,β-pyrrole-H), 9.32 (d, 2H,*J* = 5.0 Hz, β-pyrrole-H), 10.17 ppm (s, 1H, meso-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 55.06 ($2\times C_{OCH3}$), 104.22, 112.95, 118.91, 120.25, 127.38, 131.01, 134.33, 135.06, 142.67, 154.87, 157.62 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 414 (5.17), 445 (4.06), 508 (4.17), 542 (3.61), 582 (3.64), 655 nm (3.39); MS (EI, 80 eV): *m/z* (%): 614 (38) [M^+], 307 (40) [M^{++}]; HRMS [$C_{40}H_{30}N_4O_3$] : calcd 614.2317, found 614.2288.

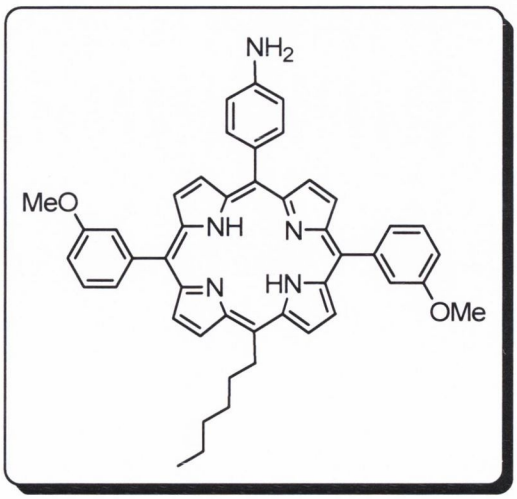
5-(4-Aminophenyl)-10,20-bis(*m*-methoxyphenyl)porphyrin 128



4-Bromoaniline (1 g, 5.8 mmol) was dissolved in 20 mL of absolute diethylether in a septum-equipped Schlenk flask under argon. The solution was cooled in an ice bath. *n*-Butyllithium (7 ml of a 2.5 M solution, 17.5 mmol) was added dropwise *via* a syringe through the septum over a period of approximately 1 h. The reaction mixture was stirred for 1 h in the ice bath and then for 45 min at 20 °C. The ethereal solution of this organometallic compound was cooled to −70 °C. To this solution was added, under argon, a cooled (−70 °C) suspension of 210 mg (0.4 mmol) of 5,15-bis(3-methoxyphenyl)porphyrin **107** in 30 mL of absolute THF. The cold bath was removed and the reaction mixture was stirred for 60 min at 20 °C. The solution gradually changed its color from red to green-brown. Water (4 mL) was added and the solution was then stirred for 20 min. On addition of water the reaction mixture changed its color to dark-green. After this time, a solution of 10 equivalents of DDQ in THF (0.06 M) was added, upon which

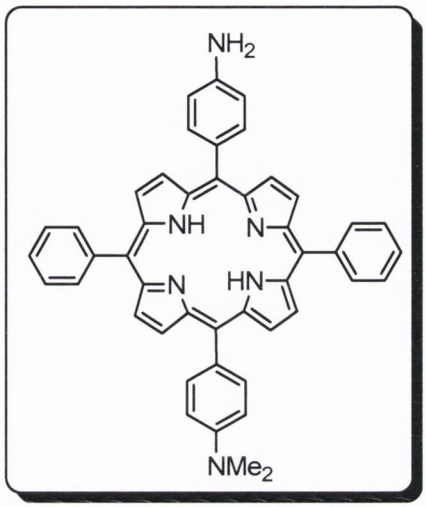
the solution became dark red again. After 15 min, the reaction mixture was filtered through silica (3×50 cm), washing with dichloromethane. The eluted porphyrin fractions were evaporated until a viscous brown oil was obtained which was then dried in vacuo at 75 °C for 3 h to remove aniline. The product was purified by column chromatography on silica (3×60 cm) using dichloromethane/methanol (20:1, v/v) as eluent. The porphyrin was redissolved in as little dichloromethane as possible and then layered with a 2–3-fold excess of methanol. After 24 h, the precipitated solid was removed by suction filtration through a D_3 frit and dried in vacuo to yield the title compound (180 mg, 0.29 mmol, 73 %) of an amorphous purple solid: mp 272 °C; R_f = 0.6 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −3.01 (s, 2H, N*H*), 3.98 (s, 6H, OCH_3), 4.80 (s, br., 2H, NH_2), 7.02 (m, 2H, 5-Ph-H), 7.31 (m, 2H, 10,20-Ph-H), 7.63 (m, 2H, 10,20-Ph-H), 7.83 (m, 4H, 10,20-Ph-H), 7.97 (m, 2H, 5-Ph-H), 8.91 (2d, *J* = 5.0 Hz, 4H, β-pyrrole-H2,8,12,18), 9.03 (d, *J* = 5.0 Hz, 2H, β-pyrrole-H3,7), 9.29 (d, *J* = 5 Hz, 2H, b-pyrrole-H13,17), 10.16 ppm (s, 1H, 15-meso-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.50, 104.41, 105.30, 113.28, 113.52, 119.21, 120.63, 121.30, 127.57, 127.78, 130.47, 131.09, 131.34, 131.64, 132.76, 135.58, 143.22, 146.01, 146.66, 152.81, 153.61, 158.09 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 369 (4.44), 397 (4.97), 415 (5.53), 483 (3.55), 511 (4.25), 546 (3.80), 585 (3.72), 638 nm (3.42); MS (EI, 80 eV, 280 8C), m/z (%): 613 (100) [M^+], 307 (%) [M^{++}]; HRMS (EI) [$C_{40}H_{31}N_5O_2$]: calcd 613.24778, found [M + 1] 614.2566.

5-(4-Aminophenyl)-15-hexyl-10,20-bis(*m*-methoxyphenyl)porphyrin 130



n-Hexyllithium (1.3 ml of a 2.5 M solution in hexane, 2.6 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-(*p*-Aminophenyl)-10,20-bis(*m*-methoxyphenyl)porphyrin **128** (50 mg, 0.081 mmol) in 40 ml of dry THF at −80 °C. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 1 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) yielding the title compound (27 mg, 0.038 mmol, 47 %) as purple crystals, besides starting material **128** (11 %); mp >300 °C; R_f = 0.63 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.93 (t, *J* = 7.2, 3H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.26 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.51 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.82 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.56 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.99 (s, 6H, OCH_3), 4.01 (s, 2H, NH_2), 5.03 (t, 2H, *J* = 8.1, $CH_2CH_2CH_2CH_2CH_2CH_3$), 6.82 (d, 2H, 10,20-Ph-H), 7.03 (d, 2H, *J* = 7.5, 5-Ph-H), 7.26 (m, 2H, 10,20-Ph-H), 7.80 (m, 4H, 10,20-Ph-H), 7.97 (d, 2H, *J* = 7.5, 5-Ph-H), 8.82 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 8.88 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 8.95 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.47 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 13.71 (15^6-C), 22.25 (15^5-C), 29.80 (15^4-C), 31.47 (15^3-C), 35.04 (15^2-C), 38.30 (15^1-C), 55.92($2\times C_{OCH3}$), 113.47, 115.68, 115.68, 117.59, 121.12, 127.78, 130.03, 132.78, 155.19. 158.31 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 420 (5.04), 516 (3.91), 555 (3.73), 593 (3.61), 653 (3.60); MS (EI, 80 eV) : *m/z* (%): 697 (16) [M^+], 626 (48) [$M^+-C_5H_{11}$], 612 (10) [$M^+ -C_5H_{11}-CH_2$], 582 (8) [$M^+ -C_5H_{11}-2\times CH_2-NH_2$], 349 (100) [$M^{++}$]; HRMS [$C_{46}H_{43}N_5O_2$] : calcd 697.3416, found 697.3395.

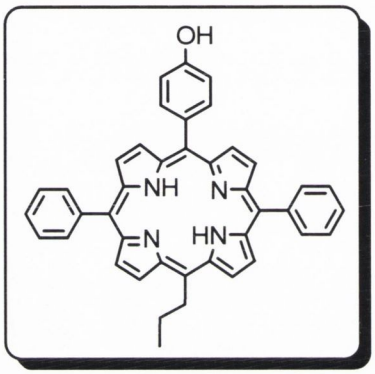
5-(4-Aminophenyl)-10,20-diphenyl-15-(*p*-dimethylaminophenyl)porphyrin 131



n-Butyllithium (0.6 ml of a 2.5 M solution in hexane, 0.6 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-(dimethylamino)bromobenzene (0.25g, 1.25 mmol) in 10 ml of dry diethylether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for another 1 h at room temperature. The solution became bright yellow and opaque. To the vigorously stirred mixture was added rapidly a solution of 5-(*p*-aminophenyl)-10,20-diphenylporphyrin **127** (50 mg, 0.09 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. The reaction mixture was stirred for 4 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Merck) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 2, v/v) and yielded the title compound (12 mg, 0.017 mmol, 20 %) as purple crystals, besides starting material **127** (18 %); mp >300 °C; R_f = 0.72 (ethyl acetate/*n*-hexane, 1 : 1, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.65 (s, 2H, NH), 3.23 (s, 6H, N(CH_3)$_2$), 7.02 (d, 2H, *J* = 7.5, Ph-H), 7.11 (d, 2H, *J* = 7.5, Ph-H), 7.77 (m, 6H, Ph-H), 7.97 (d, 2H, *J* = 7.5, Ph-H), 8.07 (d, 2H, *J* = 7.5, Ph-H), 8.24 (m, 4H, Ph-H), 8.83 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 8.84 (d, 2H, *J* = 5.0 Hz, β-pyrrole-

H), 8.92 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 8.95 ppm (d, 2H, J = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 40.27 ($N(CH_3)_2$), 110.28, 113.01, 119.31, 120.54, 126.183, 127.14, 134.13, 142.03, 145.52, 149.54 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 421 (5.09), 518 (4.03), 560 (3.90), 597 (3.79), 655 nm (3.97); MS (EI, 80 eV): *m/z* (%): 658 (4) [$M^+ - CH_2$], 336 (6) [M^{++}].

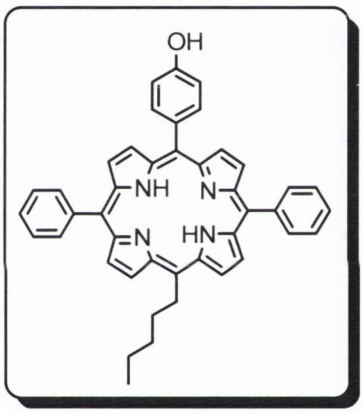
5-(*p*-Hydroxyphenyl)-10,20-diphenyl-15-propylporphyrin 135



n-Butyllithium (3 ml of a 2.5 M solution in hexane, 7.5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromophenol (0.7g, 4 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyl lithium the cold bath was removed and stirring was continued for 18 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5,15-diphenylporphyrin **42** (100 mg, 0.23 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. After 1 h the solution was treated with 0.7 propyl iodide (7.1 mmol) and stirring for 12 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 5, v/v) and yielded the title compound (56 mg, 0.09 mmol, 43 %) as purple crystals, besides trisubstituted porphyrin (24 %); mp >300 °C; R_f = 0.81 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 1.32 (t, 3H, J = 7.2 Hz, $CH_2CH_2CH_3$), 2.62 (m,

2H, $CH_2CH_2CH_3$), 5.01 (t, 2H, $J = 7.5$ Hz, $CH_2CH_2CH_3$), 6.83 (d, 2H, $J = 7.5$ Hz, Ph-H), 7.77 (m, 6H, Ph-H), 7.81 (s, 1H, O*H*), 7.96 (d, 2H, $J = 7.5$ Hz, Ph-H), 8.24 (m, 4H, Ph-H), 8.85 (m, 4H, β-pyrrole-H), 8.98 (d, 2H, $J = 5.0$ Hz, β-pyrrole-H), 9.49 ppm (d, 2H, $J = 5.0$ Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): $\delta = 14.89$ (15^3-C), 31.65 (15^2-C), 37.30 (15^1-C), 113.52, 119.22, 119.52, 120.22, 126.59, 127.63, 134.49, 135.50, 142.44, 155.21 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε)=418 (5.05), 515 (3.70), 552 (3.40), 594 (3.02), 656 nm (3.52); MS (EI, 80 eV): *m/z* (%): 596 (18) [M^+], 567 (70) [$M^+ - C_2H_5$], 299 (28) [M^{++}+H]; HRMS [$C_{41}H_{32}N_4O$]: calcd 596.2576, found 596.2562.

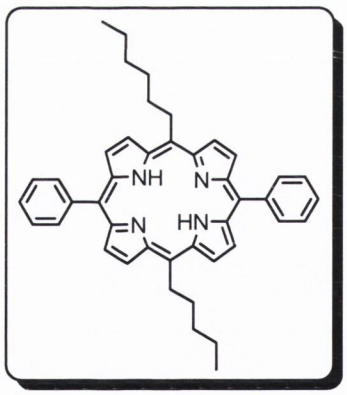
5-(*p*-Hydroxyphenyl)-15-pentyl-10,20-diphenylporphyrin 136



n-Butyllithium (3 ml of a 2.5 M solution in hexane, 7.5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromophenol (0.7g, 4 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 18 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5,15-diphenylporphyrin **42** (150 mg, 0.35 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. After 1 h the solution was treated with 0.8 *n*-pentyl iodide (6.1 mmol) and stirring for 12 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification

was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) and yielded the title compound (81 mg, 0.13 mmol, 40 %) as purple crystals, besides trisubstituted porphyrin (22 %); mp >300 °C; R_f = 0.66 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.98 (t, 3H, *J* = 7.2 Hz, $CH_2CH_2CH_2CH_2CH_3$), 1.52 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 1.80 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 2.56 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 4.99 (t, 2H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_2CH_3$), 7.03 (d, 2H, *J* = 7.5 Hz, Ph-H), 7.75 (s, 1H, O*H*), 7.78 (m, 6H, Ph-H), 8.01 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.24 (m, 4H, Ph-H), 8.81 (m, 4H, β-pyrrole-H), 8.93 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.48 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H) ppm; ^{13}C NMR (60 MHz, $CDCl_3$): δ = 13.69 (15^5-C), 22.33 (15^4-C), 29.27 (15^3-C), 32.28 (15^2-C), 38.11 (15^1-C), 113.19, 115.32, 119.05, 120.13, 126.16, 127.21, 134.06, 135.16, 142.01, 154.88 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 416 (5.01), 486 (3.77), 516 (3.85), 548 (3.72), 596 (3.59), 655 nm (3.86); MS (EI, 80 eV): *m/z* (%): 624 (19) [M^+], 567 (68) [$M^+ - C_4H_9$], 312 (18) [M^{++}]; HRMS [$C_{43}H_{36}N_4O$]: calcd 624.2889, found 624.2867.

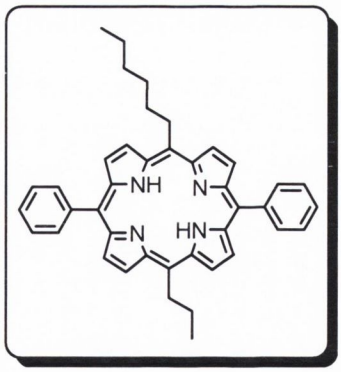
5-Hexyl-10,20-diphenyl-15-pentylporphyrin 139



n-Hexyllithium (1 ml of a 2.5 M solution in hexane) was slowly added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5,15-diphenylporphyrin **42** (100 mg, 0.23 mmol) in 40 ml of dry THF at −80 °C under an argon atmosphere. After 15 min the solution was treated with 0.8 *n*-pentyl iodide (6.1 mmol) and stirring for 24 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and

the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) and yielded the title compound (37 mg, 0.06 mmol, 27 %) as purple crystals, besides trisubstituted porphyrin (27 %); mp >300 °C; R_f = 0.73 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.66 (s, 2H, N*H*), 0.92 (m, 6H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.27 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$) 1.54 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.82 (m, 4H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 2.51 (m, 4H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.99 (m, 4H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.75 (m, 6H, Ph-H), 8.18 (m, 4H, Ph-H), 8.85 (m, 4H, β-pyrrole-H), 9.43 ppm (m, 4H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 13.68 (5^6-C), 22.01 (5^5-C), 22.27 (15^5-C), 29.27 (5^4-C), 29.78 (15^4-C), 31.47 (5^3-C), 32.25 (15^3-C), 34.82 (5^2-C), 35.20 (15^2-C), 37.93 (5^1-C), 39.94 (15^1-C), 118.45, 119.35, 126.09, 127.05, 134.00, 142.27 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 417 (4.94), 486 (3.14), 516 (2.88), 558 (3.23), 594 (3.18), 651 nm (3.30); MS (EI, 80 eV): *m/z* (%): 616 (7) [M^+], 559 (14) [$M^+-C_4H_9$], 545 (14) [$M^+-C_5H_{11}$], 488 (20) [$M^+-C_4H_9-C_5H_{11}$], 308 (10) [M^{++}]; HRMS [$C_{43}H_{44}N_4$]: calcd 616.3565, found 616.3547.

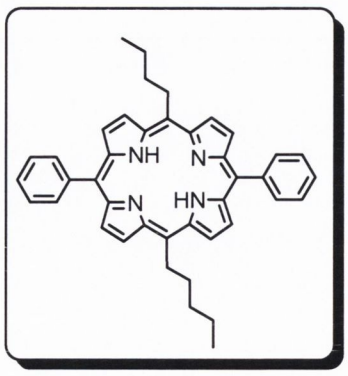
5-Hexyl-10,20-diphenyl-15-propylporphyrin 140



n-Hexyllithium (1 ml of a 2.5 M solution in hexane) was slowly added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5,15-diphenylporphyrin **42** (100 mg, 0.23 mmol) in 40 ml of dry THF at −80 °C under an argon atmosphere. After 15 min the solution was treated with 0.8 ml propyl iodide (8.1 mmol) and stirring for 24 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added

for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 6, v/v) and yielded the title compound (40 mg, 0.07 mmol, 31 %) as purple crystals, besides trisubstituted porphyrin (22 %); mp >300 °C; R_f = 0.72 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.66 (s, 2H, N*H*), 0.92 (m, 6H, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.28 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$) 1.52 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.82 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.51 (m, 4H, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.99 (m, 4H, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.78 (m, 6H, Ph-H), 8.19 (m, 4H, Ph-H), 8.87 (m, 4H, β-pyrrole-H), 9.41 ppm (m, 4H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 14.55 (5^6-C), 15.32 (15^3-C), 23.12 (5^5-C), 29.79 (5^4-C), 30.11 (5^3-C), 30.63 (15^2-C), 32.32 (5^2-C), 37.59 (5^1-C), 39.10 (15^1-C), 119.32, 119.86, 120.26, 126.95, 128.01, 134.85, 143.12, 143.87, 145.82 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 417 (4.99), 486 (2,86), 516 (3.46), 551 (2.94), 594 (2.46), 656 nm (3.25); MS (EI, 80 eV): *m/z* (%): 588 (16) [M^+], 559 (20) [$M^+-C_2H_5$], 517 (50) [$M^+-C_5H_{11}$], 488 (30) [$M^+-C_2H_5-C_5H_{11}$], 294 (14) [M^{++}]; HRMS [$C_{41}H_{40}N_4$]: calcd 588.3252, found 588.3248.

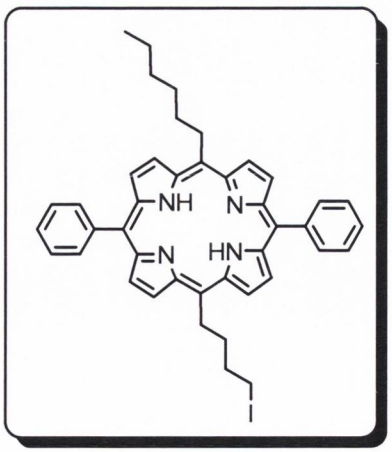
5-Butyl-10,20-diphenyl-15-pentylporphyrin 141



n-Butyllithium (0.4 ml of 2.5 M solution in hexane, 1 mmol) was slowly added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5,15-diphenylporphyrin **42** (200 mg, 0.46 mmol) in 40 ml of dry THF at −80 °C under an argon atmosphere. After 15 min

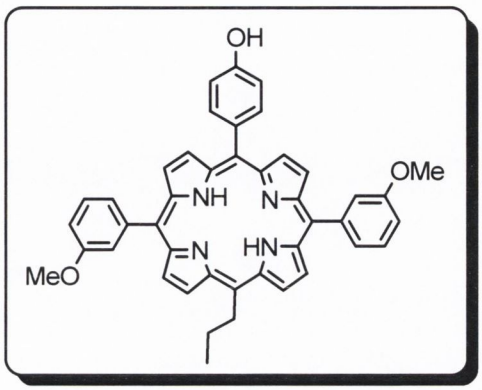
the solution was treated with 0.1 *n*-pentyl iodide (0.6 mmol) and stirring for 12 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) and yielded the title compound (87 mg, 0.14 mmol, 34 %) as purple crystals, besides trisubstituted porphyrin (20 %); mp >300 °C; R_f = 0.46 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.95 (t, 3H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_2CH_3$), 1.11 (t, 3H, *J* = 7.5 $CH_2CH_2CH_2CH_3$), 1.29 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 1.78 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 2.54 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 4.96 (t, 4H, *J* = 7.8, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 7.73–7.79 (m, 6H, Ph-H), 8.18–8.21 (m, 4H, Ph-H), 8.85–8.87 (m, 4H, β-pyrrole-H), 9.41–9.43 ppm (m, 4H, β-pyrrole-H); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 417 (4.96), 438 (3.76), 486 (3.65), 516 (3.73), 552 (3.55), 595 (3.43), 650 nm (3.43); MS (EI, 80 eV): *m/z* (%): 588 (80) [M^+], 545 (60) [$M^+ - C_3H_7$], 531 (100) [$M^+ - C_4H_9$], 488 (52) [$M^+ - C_4H_9 - C_3H_7$], 295 (40) [M^{++}]; HRMS [$C_{41}H_{40}N_4$]: calcd 588.3252, found 588.3235.

5-Hexyl-10,20-diphenyl-15-(4-iodobutyl)porphyrin 142



n-Hexyllithium (1 ml of a 2.5 M solution in hexane) was slowly added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5,15-diphenylporphyrin **42** (120 mg, 0.26 mmol) in 40 ml of dry THF at −80 °C under an argon atmosphere. After 15 min the solution was treated with 0.2 ml 1,4-diiodobutane (0.6 mmol) and stirring for 12 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) and yielded the title compound (33 mg, 0.045 mmol, 21 %) as purple crystals, besides trisubstituted porphyrin (15 %) and starting material **42** (8 %); mp >300 °C; R_f = 0.69 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.15 (s, 2H, N*H*), δ = 0.91 (t, 3H, *J* = 7.2 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.26 (m, 4H, $CH_2CH_2CH_2CH_2I$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.33 (m, 2H, $CH_2CH_2CH_2CH_2I$), 1.54 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.65 (m, 2H, $CH_2CH_2CH_2CH_2I$), 1.88 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.66 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.24 (m, 2H, $CH_2CH_2CH_2CH_2I$), 5.05 (t, 2H, *J* = 8.4 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.66 (m, 6H, Ph-H), 8.02 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H) 8.22 (m, 4H, Ph-H), 8.53 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 8.97 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.58 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H)); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 10.96 (15^2-C), 14.04 (15^3-C), 14.16 (5^6-C), 22.74 (5^5-C), 28.92 (15^1-C), 29.69 (5^4-C), 30.36 (5^3-C), 31.21 (15^4-C), 31.96 (5^2-C), 38.74 (5^1-C), 116.68, 120.41, 126.54, 134.36, 142.22, 145.44, 149.38, 152.38, 156.23 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 417 (5.12), 486 (3.73), 515 (3.81), 552 (3.46), 596 (3.35), 650 nm (2.98); MS (EI, 80 eV) : *m/z* (%): 728 (16) [M^+], 600 (12) [M^+−H−I].

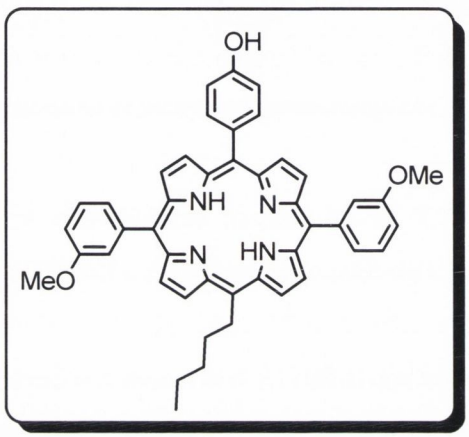
5-(*p*-Hydroxyphenyl)-10,20-bis(*m*-methoxyphenyl)-15-propylporphyrin 143



n-Butyllithium (2 ml of a 2.5 M solution in hexane, 5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromophenol (0.43g, 2.5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 18 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5,15-bis-(*m*-methoxyphenyl)porphyrin **107** (150 mg, 0.28 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. After 1 h the solution was treated with 0.7 ml *n*-propyl iodide (7.1 mmol) and stirring for 12 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 5, v/v) and yielded the title compound (110 mg, 0.167 mmol, 58 %) as purple crystals, besides trisubstituted porphyrin (13 %); mp >300 °C; R_f = 0.57 (ethyl acetate/*n*-hexane, 1 : 3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 1.32 (t, 3H, *J* = 7.2 Hz, $CH_2CH_2CH_3$), 2.60 (m, 2H, $CH_2CH_2CH_3$), 3.98 (s, 6H, OCH_3), 5.03 (t, 2H, *J* = 8.1 Hz, $CH_2CH_2CH_3$), 7.35 (d, 2H, *J* = 7.5 Hz, Ph-H), 7.63 (m, 2H, Ph-H), 7.69 (m, 2H, Ph-H), 7.84 (m, 4H, Ph-H), 7.89 (s, 1H, O*H*), 7.94 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.82 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 8.88 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.01 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.49 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 14.89 (15^3-C), 31.65

(15^2-C), 37.27 (15^1-C), 55.47 ($2\times C_{OCH3}$), 113.49, 114.95, 119.23, 120.48, 127.41, 127.67, 134.02, 135.46, 143.75, 155.34, 157.86 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 418 (4.99), 485 (3.71), 515 (3.82), 551 (3.63), 594 (3.39), 656 nm (3.59); MS (EI, 80 eV): *m/z* (%): 656 (4) [M^+], 627 (8) [$M^+-C_2H_5$]; HRMS [$C_{43}H_{36}N_4O_3$]: calcd 656.2787, found 656.2766.

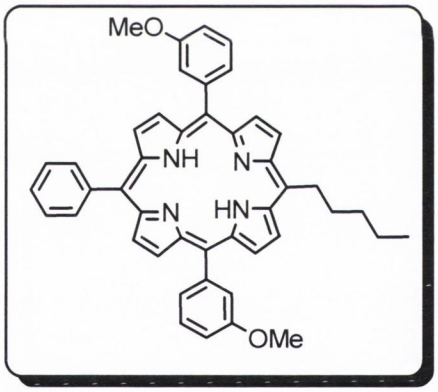
5-(*p*-Hydroxyphenyl)-10,20-bis(*m*-methoxyphenyl)-15-pentylporphyrin 144



n-Butyllithium (2 ml of a 2.5 M solution in hexane, 5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromophenol (0.43g, 2.5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 18 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5,15-bis-(*m*-methoxyphenyl)porphyrin **107** (100 mg, 0.19 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. After 1 h the solution was treated with 0.8 ml *n*-pentyl iodide (6.1 mmol) and stirring for 12 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 2, v/v) yielded the title compound (48 mg, 0.07 mmol, 36 %) as purple crystals, besides trisubstituted porphyrin (18 %); mp >300 °C; R_f = 0.55 (ethyl acetate/*n*-hexane, 1 : 1, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.99 (t, 3H, *J* = 7.2 Hz,

$CH_2CH_2CH_2CH_2CH_3$), 1.31 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.75 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.60 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.01 (s, 6H, OCH_3), 5.03 (t, 2H, J = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_3$), 6.64 (d, 2H, J = 7.5 Hz, Ph-H), 6.95–7.04 (m, 2H, Ph-H), 7.35–7.38 (m, 2H, Ph-H), 7.63–7.86 (m, 4H, Ph-H), 7.82 (s, 1H, O*H*), 7.96 (d, 2H, J = 7.5 Hz, Ph-H), 8.82 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 8.88 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 9.01 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 9.49 ppm (d, 2H, J = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 14.52 (15^5-C), 23.17 (15^4-C), 33.12 (15^3-C), 35.88 (15^2-C), 38.94 (15^1-C), 55.92 ($2\times C_{OCH3}$), 113.03, 114.03, 115.50, 117.48, 119.64, 121.03, 127.83, 129.17, 132.69, 134.82, 135.98, 144.19, 153.91, 155.69, 158.30 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 418 (5.05), 448 (4.12), 515 (3.87), 595 (3.71), 650 nm (3.64); MS (EI, 80 eV): *m/z* (%): 684 (8) [M^+], 627 (10) [$M^+-C_4H_9$], 342 (11) [M^{++}]; HRMS [$C_{45}H_{40}N_4O_3$]: calcd 684.3100, found 684.3085.

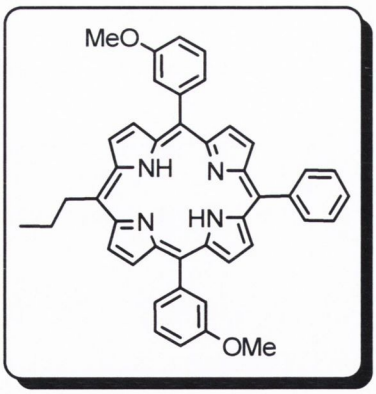
5,15-Bis(*m*-methoxyphenyl)-10-Pentyl-20-phenyl-porphyrin 146



Phenyllithium (2 ml of a 1.8 M solution in hexane, 0.06 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5,15-bis(*m*-methoxyphenyl)porphyrin **107** (200 mg, 0.38 mmol) in 40 ml of dry THF. The mixture was heated to 50 °C and stirred for 30 min. After 1 h the solution was treated with 0.8 ml *n*-pentyl iodide (6.1 mmol) and stirring for 20 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the

mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 2, v/v) yielded the title compound (105 mg, 0.157 mmol, 41 %) as purple crystals, besides trisubstituted porphyrin (16 %); mp >300 °C; R_f = 0.76 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.67 (s, 2H, N*H*), 1.02 (t, 3H, *J* = 7.2 Hz, $CH_2CH_2CH_2CH_2CH_3$), 1.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 1.81 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 2.58 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 4.01 (s, 6H, OCH_3), 5.01 (t, 2H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_3$), 7.38 (m, 2H, Ph-H), 7.63−7.85 (m, 9H, Ph-H), 8.21 (m, 2H, Ph-H), 8.83 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 8.87 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 8.98 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.48 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 13.69 (5^5-C), 22.33 (5^4-C), 32.28 (5^3-C), 35.04 (5^2-C), 38.11 (5^1-C), 55.06 ($2\times C_{OCH3}$), 113.08, 118.82, 120.01, 120.29, 126.27, 126.96, 134.08, 141.65, 143.33, 157.48 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε)=417 (5.05), 486 (3.35), 514 (3.71), 550 (3.35), 592 (3.02), 656 nm (3.32); MS (EI, 80 eV): *m/z* (%):653 (3) [M^+-CH_3], 334 (10) [M^{++}]; HRMS [$C_{45}H_{40}N_4O_2$]: calcd 668.3151, found 668.3122.

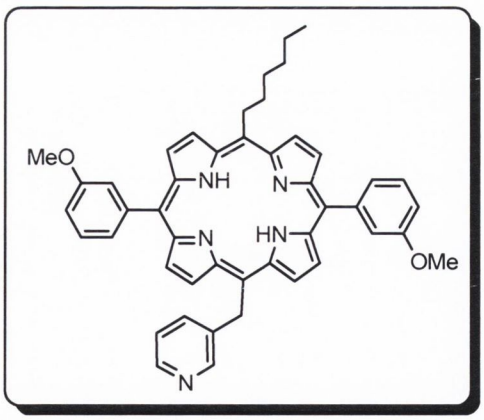
5,15-Bis(*m*-methoxyphenyl)-10-phenyl-20-propylporphyrin 147



Phenyllithium (2 ml of a 1.8 M solution in hexane, 0.06 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5,15-bis(*m*-methoxyphenyl)porphyrin **107** (150 mg, 0.285 mmol) in 40 ml of dry THF. The mixture was heated to 50 °C and stirred for 30 min. After 1 h the solution was treated with 0.7 ml *n*-propyl iodide (7.1 mmol) and stirring for 20 h and heating to 70 °C (TLC control). Subsequently, a

mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 4, v/v) yielded the title compound (32 mg, 0.05 mmol, 24 %) as purple crystals, besides trisubstituted porphyrin (14 %); mp >300 °C; R_f = 0.73 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.71 (s, 2H, N*H*), 1.34 (t, 3H, *J* = 7.2 Hz, $CH_2CH_2CH_3$), 2.62 (m, 2H, $CH_2CH_2CH_3$), 4.01 (s, 6H, OCH_3), 5.03 (t, 2H, *J* = 8.1 Hz, $CH_2CH_2CH_3$), 7.37 (m, 4H, Ph-H), 7.77 (m, 6H, Ph-H), 8.22 (m, 3H, Ph-H), 8.82 (m, 4H, β-pyrrole-H), 8.99 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.49 ppm (d, 2H, *J* = 5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 15.36 (15^3-C), 32.13 (15^2-C), 37.76 (15^1-C), 55.91 ($2\times C_{OCH3}$), 113.93, 119.67, 120.82, 127.12, 128.04, 134.93, 142.48, 144.17, 158.31 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 417 (5.03), 486 (3.65), 513 (3.86), 558 (3.53), 592 (3.44), 656 nm (3.55); MS (EI, 80 eV): *m/z* (%): 640 (10) [M^+], 613 (12) [$M^+-C_2H_5+2H$]; HRMS [$C_{45}H_{40}N_4O_3$]: calcd 640.2838, found 640.2849.

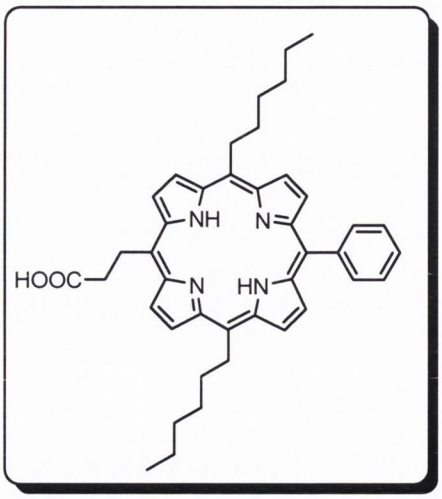
5-Hexyl-10,20-bis(*m*-methoxyphenyl)-15-[(3-pyridyl)methyl]porphyrin 155



n-Hexyllithium (1 ml of a 2.5 M solution in hexane) was slowly added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5,15-bis(*m*-methoxyphenyl)porphyrin **107** (100 mg, 0.19 mmol) in 40 ml of dry THF at −80 °C under an argon atmosphere. After 15 min the solution was treated with a solution of 300 mg (0.86

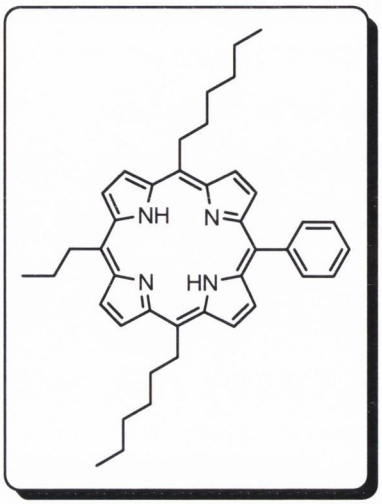
mmol) 3-(iodomethyl)pyridine hydriodide dissolved in 4 ml DMF and stirring for 24 h and heating to 75 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.04 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 8, v/v)) yielded the title compound (8 mg, 0.01 mmol, 6 %) as purple crystals, besides trisubstituted porphyrin (28 %); mp >300 °C; R_f = 0.35 (ethyl acetate/*n*-hexane, 1 : 1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.62 (s, 2H, N*H*), 0.91 (t, *J* = 7.2, 3H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.23 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.54 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.83 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.03 (s, 6H, OCH_3), 4.99 (t, 2H, *J* = 8.1, $CH_2CH_2CH_2CH_2CH_2CH_3$), 6.38 (s, 2H, Pyridyl−CH_2), 7.01 (m, 2H, Pyridyl-H), 7.35 (m, 3H, 2 Ph-H, 1 pyridyl-H), 7.66 (m, 2H, Ph-H), 7.79 (m, 4H, Ph-H), 8.38 (s, 1H, Pyridyl-H), 8.95 (m, 4H, β-pyrrole-H2,8,12,18), 9.33 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H13,17), 9.48 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H3,7); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 420 (5.07), 485 (3.74), 516 (3.62), 551 (2.92), 593 (3.04), 655 nm (4.00); HRMS [$C_{46}H_{43}N_5O_2$]: calcd 697.3416, found [M + 1] 698.3516.

3-(5,15-Dihexyl-10-phenylporphyrin-20-yl)propionic acid 156



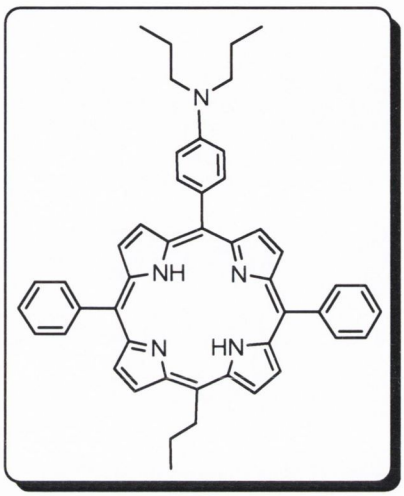
Phenyllithium (0.6 ml of a 1.8 M solution in hexane, 0.018 mmol) was slowly added under an argon atmosphere to a 50 ml Schlenk flask charged with a solution of 5,15-dihexylporphyrin **154** (80 mg, 0.167 mmol) in 30 ml of dry THF at R.T. under an argon atmosphere. After 15 min the solution was treated with a solution of 200 mg (1 mmol) 3-iodopropionic acid dissolved in 5 ml THF and stirring for 24 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) yielded the title compound (19 mg, 0.03 mmol, 18 %) as purple crystals, besides trisubstituted porphyrin (27 %); mp >300 °C; $R_f = 0.47$ (ethyl acetate/*n*-hexane, 1 : 7, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.65 (s, 2H, N*H*), 0.91 (t, 6H, J = 7.2, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.20 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.55 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.86 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.57 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, CH_2CH_2COOH) , 3.72 (t, 2H, J = 6.4, CH_2CH_2COOH), 4.98 (t, 4H, J = 8.1, $CH_2CH_2CH_2CH_2CH_2CH_3$),, 7.77 (m, 3H, Ph-H), 8.21 (m, 2H, Ph-H), 8.88 (m, 4H, β-pyrrole-H3,7,13,17), 9.44 (m, 4H, β-pyrrole-H2,8,12,18) , 10.56 (s, 1H, COO*H*); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 418 (5.08), 440 (3.94), 517 (3.79), 552 (3.91), 593 (3.88), 655 nm (4.09).

5,15-Dihexyl-10-phenyl-20-propylporphyrin 157



Phenyllithium (0.6 ml of a 1.8 M solution in hexane, 0.018 mmol) was slowly added under an argon atmosphere to a 50 ml Schlenk flask charged with a solution of 5,15-dihexylporphyrin **154** (80 mg, 0.167 mmol) in 30 ml of dry THF at R.T. under an argon atmosphere. After 15 min the solution was treated with 0.8 ml *n*-propyl iodide (8.1 mmol) and stirring for 24 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) yielded the title compound (20 mg, 0.03 mmol, 21 %) as purple crystals, besides trisubstituted porphyrin (24 %); mp >300 °C; R_f = 0.47 (ethyl acetate/*n*-hexane, 1 : 7, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.63 (s, 2H, N*H*), 0.92 (t, 6H, *J* = 7.2, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.25 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 137-1.51 (m, 7H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 1.86 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.58 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$) , 3.75 (t, 2H, *J* = 6.4, $CH_2CH_2CH_3$), 4.99 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 7.77 (m, 3H, Ph-H), 8.18 (m, 2H, Ph-H), 8.82 (d, 2H, *J* = 5 Hz, β-pyrrole-H8,12), 9.39 (d, 2H, *J* = 5 Hz, β-pyrrole-H2,18), 9.52 (d, 2H, *J* = 5 Hz, β-pyrrole-H3,17), 9.56 (d, 2H, *J* = 5 Hz, β-pyrrole-H7,13) ; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 440 (5.03), 486 (3.92), 577 (3.77), 594 (3.77), 659 nm (3.37); HRMS [$C_{43}H_{44}N_4$]: calcd 596.3878, found [M + 1] 597.3953.

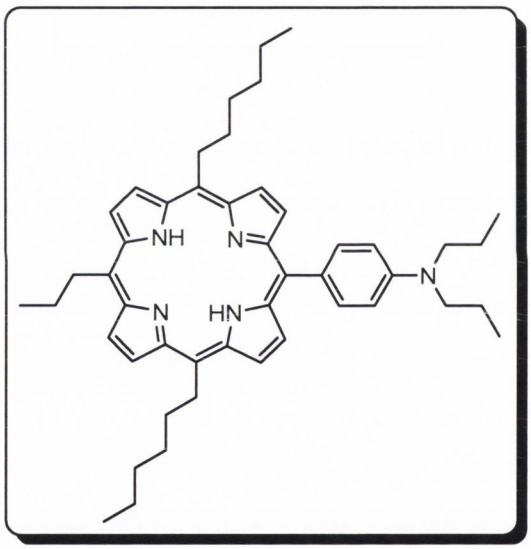
5-[*p*-(Dipropylamino)phenyl]-10,20-diphenyl-15-propylporphyrin 158



n-Butyllithium (3 ml of a 2.5 M solution in hexane, 7.5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromoaniline (0.5g, 2.5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for another 2 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5,15-diphenylporphyrin **42** (100 mg, 0.22 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. After 1 h the solution was treated with 1 ml *n*-propyl iodide (10 mmol) and stirring for 12 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 5, v/v) yielded the title compound (53 mg, 0.078 mmol, 36 %) as purple crystals, besides starting material (15 %); mp >300 °C; R_f = 0.57 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −2.64 (s, 2H, N*H*), 1.11 (m, 6H, $N(CH_2CH_2CH_3)_2$, 1.33 (t, 2H, *J* = 7.2 Hz, $CH_2CH_2CH_3$), 1.82 (m, 4H, $N(CH_2CH_2CH_3)_2$), 2.57 (m, 2H, $CH_2CH_2CH_3$), 3.49 (m, 4H, $N(CH_2CH_2CH_3)_2$), 5.01 (t, 2H, *J* = 8.1 Hz, $CH_2CH_2CH_3$), 7.02 (d, 2H, *J* = 7.5 Hz, Ph-H), 7.77 (m, 6H, Ph-H), 8.03 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.21 (m,

4H, Ph-H), 8.77 (d, 2H, $J = 5.0$ Hz, β-pyrrole-H), 8.89 (d, 2H, $J = 5.0$ Hz, β-pyrrole-H), 8.96 (d, 2H, $J = 5.0$ Hz, β-pyrrole-H), 9.46 (d, 2H, $J = 5.0$ Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 13.69 (15^3-C), 20.09 ($N(CH_2CH_2\mathbf{C}H_3)_2$), 29.26 ($N(CH_2\mathbf{C}H_2CH_3)_2$), 31.19 ($15^2$-C), 36.83 ($15^1$-C), 39.70 ($N(\mathbf{C}H_2CH_2CH_3)_2$), 109.58, 118.81, 121.51, 126.12, 127.11, 134.10, 135.61, 142.24 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 417 (5.15), 517 (4.21), 558 (3.75), 594 (3.16), 652 nm (3.73); MS (EI, 80 eV): *m/z* (%): 678 (36) [M^+–H], 664 (48) [M^+–CH_3], 650 (6) [M^+–C_2H_5], 622 (5) [M^+–C_2H_5–CH_3–CH_3+2H], 592 (6) [M^+–3(C_2H_5)], 578 (44) [M^+–H–$N(CH_2CH_2CH_3)_2$].

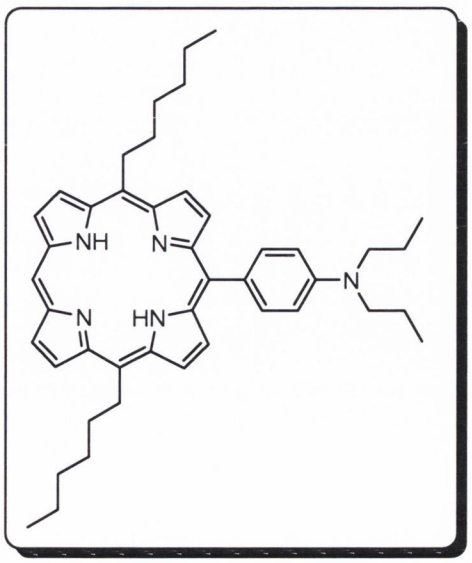
5,15-Dihexyl-10-[*p*-(dipropylamino)phenyl]-20-propylporphyrin 159



n-Butyllithium (4 ml of a 2.5 M solution in hexane, 10 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromoaniline (1 g, 5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for another 2 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5,15-dihexylporphyrin **154** (150 mg, 0.313 mmol) in 40 ml of dry THF under an argon atmosphere. The mixture changed from deep purple to brown within 30 min. After 1 h the solution was treated with 1 ml propyl iodide (10 mmol) and stirred for 12 h and heated to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was

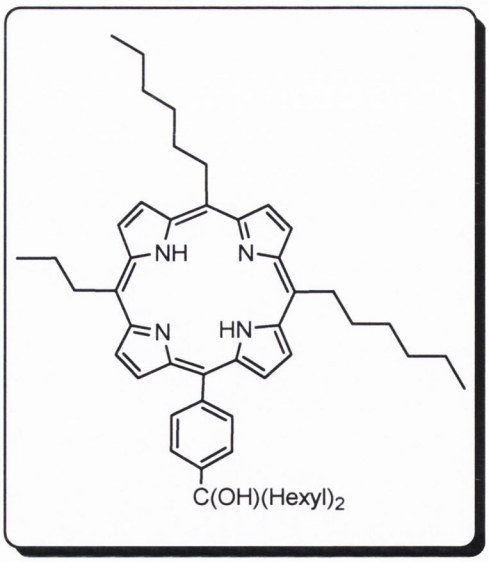
stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v). The first fraction consisted of **159** (43 mg, 0.06 mmol, 20 %) and the second fraction of **160** (34 mg, 0.05 mmol, 16 %). **159:** purple crystals, mp >300 °C; $R_f = 0.63$ (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta = -2.57$ (s, 2H, N*H*), 0.92 (t, 6H, $J = 7.2$ Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.11 (m, 6H, $N(CH_2CH_2CH_3)_2$, 1.25 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.37-1.51 (m, 7H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 1.84-1.93 (m, 8H, $CH_2CH_2CH_2CH_2CH_3$, $N(CH_2CH_2CH_3)_2$), 2.56 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 3.55 (m, 4H, $N(CH_2CH_2CH_3)_2$), 4.99 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 7.04 (d, 2H, $J = 7.5$ Hz, Ph-H), 8.05 (d, 2H, $J = 7.5$ Hz, Ph-H), 9.02-9.11 (m, 4H, β-pyrrole-H), 9.45 (m, 4H, β-pyrrole-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=11.22, 13.76, 14.59, 20.13, 20.24, 22.34, 29.22, 29.85, 31.27, 31.52, 32.63, 34.56, 35.03, 37.15, 38.16, 38.21, 50.71, 52.74, 109.24, 109.44, 117.84, 118.35, 118.57, 126.48, 127.55, 128.86, 146.52 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 436 (5.10), 486 (4.32), 511 (4.29), 581 (3.64), 656 nm (4.28); HRMS [$C_{47}H_{61}N_5$]: calcd 695.4926, found [M + 1] 696.5008.

5,15-Dihexyl-10-[*p*-(dipropylamino)phenyl]-porphyrin 160



This fraction was obtained from the reaction leading to **159**; purple crystals, mp >300 °C; R_f = 0.55 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.75 (s, 2H, N*H*), 0.92 (t, 6H, *J* = 7.2, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.14 (m, 6H, $N(CH_2CH_2CH_3)_2$, 1.28 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.37-1.51 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.85-1.94 (m, 8H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $N(CH_2CH_2CH_3)_2$), 2.58 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.56 (m, 4H, $N(CH_2CH_2CH_3)_2$), 5.02 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.04 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.04 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.99 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.34 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 8.44 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 9.56 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H), 10.03 ppm (s, 1H, 20-meso-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.22, 13.74, 20.23, 22.31, 29.29, 29.82, 31.51, 34.55, 38.15, 52.75, 102.72, 109.26, 118.57, 120.45, 126.46, 127.58, 129.33, 130.91, 131.91, 135.36, 144.73, 147.23, ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε)=434 (5.11), 585 (3.78), 656 nm (4.11); HRMS [$C_{44}H_{55}N_5$]: calcd 653.4457, found [M + 1] 654.4556.

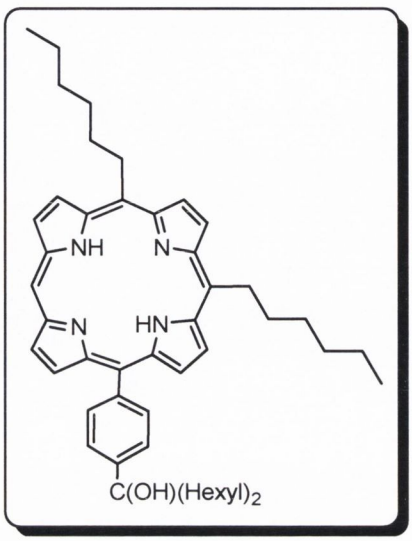
5,10-Dihexyl-15-[4-(dihexyl-hydroxymethyl)phenyl]-20-propylporphyrin 166



n-Hexyllithium (2 ml of a 2.5 M solution in hexane, 5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-hexyl-15-(4-methylcarboxyphenyl)porphyrin **165** (40 mg, 0.07 mmol) in 40 ml of dry THF under an argon

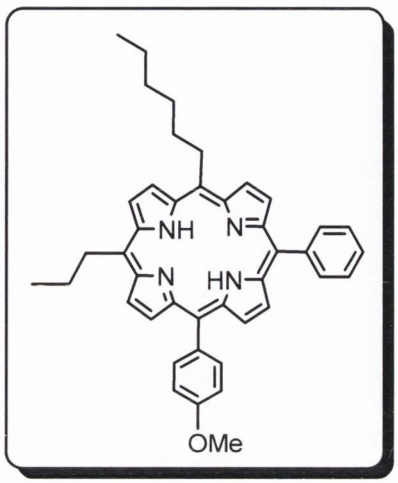
atmosphere. The mixture changed from deep purple to brown within 30 min. After 1 h the solution was treated with 0.5 ml propyl iodide (0.52 mmol) and stirring for 12 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.02 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with acetone/*n*-hexane (1 : 5, v/v). The first fraction consisted of **166** (11 mg, 0.013 mmol, 18 %) and the second fraction of **167** (8 mg, 0.01 mmol, 14 %). **166:** purple crystals, mp >300 °C; R_f = 0.31 (acetone/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.60 (s, 2H, N*H*), 0.96-1.15 (t, 12H, *J* = 7.2, $CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$), 1.23 (m, 8H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$), 1.41-1.65 (m, 16H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$), 1.81-1.91 (m, 7H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 2.12 (m, 4H, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$), 2.55 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 4.98 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 7.78 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.17 (m, 6H, Ph-H), 8.87 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H13,17), 9.43 (m, 2H, β-pyrrole-H2,18), 9.54 (m, 4H, β-pyrrole-H3,7,8,12); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.67, 22.20, 22.38, 23.29, 28.99, 29.31, 31.52, 35.01, 35.38. 36.84, 38.28, 38.47, 42.82, 117.61, 118.28, 118.68, 118.90, 123.10, 126.83, 127.35, 127.88, 133.74, 140.02, 145.33 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 418 (5.18), 519 (3.50), 553 (3.78), 601 (3.88), 655 nm (3.75); HRMS [$C_{54}H_{74}N_4O$]: calcd 794.5862, found [M + 1] 795.5645.

5,10-Dihexyl-15-[4-(dihexyl-hydroxymethyl)phenyl]-porphyrin 167



This fraction was obtained from the reaction leading to **166**; purple crystals, mp >300 °C; R_f = 0.31 (acetone/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.88 (s, 2H, N*H*), 0.93-1.15 (t, 12H, *J* = 7.2 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$), 1.23 (m, 8H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$), 1.41-1.73 (m, 16H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$), 1.82-1.90 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.09 (m, 4H, $C(OH)CH_2CH_2CH_2CH_2CH_2CH_3$), 2.57 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 5.06 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.79 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.21 (d, 2H, *J* = 7.5 Hz, Ph-H), 8.87 (d, 2H, *J* = 5.0 Hz, β-pyrrole-H13,17), 9.34 (2d, 2H, β-pyrrole-H2,18), 9.54 (m, 4H, β-pyrrole-H3,7,8,12), 10.03 ppm (s, 1H, 20-meso-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.66, 22.18, 29.29, 29.88, 29.90, 31.31, 34.87, 35.66, 38.37, 38.64, 42.80, 103.03, 117.77, 119.06, 120.08, 123.29, 127.81, 130.38, 133.91, 138.72, 139.38, 145.41 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 435 (5.10), 486 (3.11), 514 (2.57), 581 (3.42), 656 nm (3.72); HRMS [$C_{51}H_{68}N_4O$]: calcd 752.5393, found [M + 1] 753.5416.

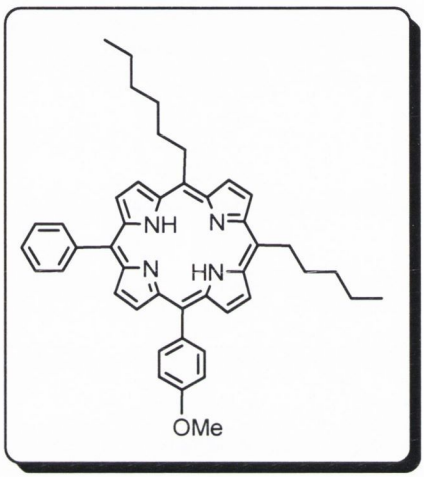
5-Hexyl-10-phenyl-15-(4-methoxyphenyl)-20-propylporphyrin 175



Phenyllithium (0.8 ml of a 1.8 M solution in hexane, 0.02 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-hexyl-15-(4-methoxyphenyl)porphyrin **170** (100 mg, 0.19 mmol) in 40 ml of dry THF. The mixture was heated to 50 °C and stirred for 30 min. After 1 h the solution was treated with 0.7 propyl iodide (7.1 mmol) and stirring for 20 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) yielded the title compound (31 mg, 0.05 mmol, 25 %) as purple crystals, besides trisubstituted porphyrin (14 %) and starting material **170** (8 %); mp >300 °C; R_f = 0.76 (ethyl acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.61 (s, 2H, N*H*), 0.99 (t, 6H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 1.34 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$) 1.41 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.86 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.57 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 4.09 (s, 3H, OCH_3), 5.02 (t, 4H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 7.25 (d, 2H, *J* = 8 Hz, Ph-H), 7.79 (m, 3H, Ph-H), 8.15 (d, 2H, *J* = 8 Hz, Ph-H), 8.27 (m, 2H, Ph-H), 8.81 (m, 2H, β-pyrrole-H13,17), 8.98 (m, 2H, β-pyrrole-H2,18), 9.43 (m, 2H, β-pyrrole-H3,12), 9.56 (m, 2H, β-pyrrole-H7,8); ^{13}C NMR

(100 MHz, $CDCl_3$): δ = 13.79, 14.58, 22.36, 29.33, 29.88, 31.33, 31.53, 35.25, 37.10, 38.45, 55.12, 111.71, 118.16, 119.24, 119.49, 126.22, 126.75, 127.13, 128.35, 134.07, 135.14, 141.99, 158.86 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 444 (4.97), 487 (4.30), 601 (4.03), 657 nm (4.28); HRMS [$C_{42}H_{42}N_4O$]: calcd 618.3358, found [M + 1] 619.3425.

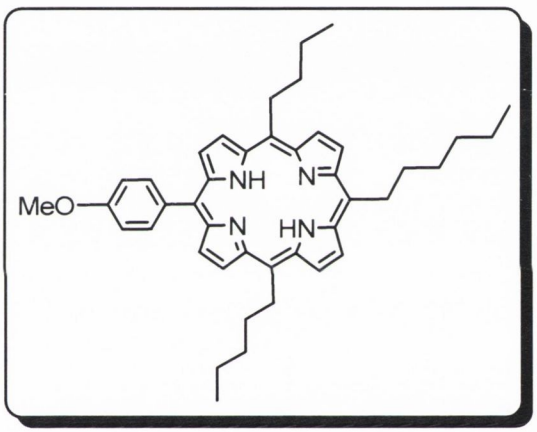
5-Hexyl-10-pentyl-15-(4-methoxyphenyl)-20-phenylporphyrin 176



Phenyllithium (0.8 ml of a 1.8 M solution in hexane, 0.02 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-hexyl-15-(4-methoxyphenyl)porphyrin **170** (100 mg, 0.19 mmol) in 40 ml of dry THF. The mixture was heated to 50 °C and stirred for 30 min. After 1 h the solution was treated with 0.8 ml pentyl iodide (6.1 mmol) and stirred for 20 h and heated to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) yielded the title compound (18 mg, 0.027 mmol, 14 %) as purple crystals, besides trisubstituted porphyrin (9 %) and starting material **170** (6 %); mp >300 °C; R_f = 0.75 (ethyl acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.64 (s, 2H, N*H*), 0.98 (t, 6H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 1.43 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$) 1.58 (m, 4H,

$CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 1.87 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 2.59 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 4.09 (s, 3H, OCH_3), 5.03 (t, 4H, $J = 8.1$ Hz, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 7.31 (d, 2H, $J = 8$ Hz, Ph-H), 7.77 (m, 3H, Ph-H), 8.13 (d, 2H, $J = 8$ Hz, Ph-H), 8.23 (m, 2H, Ph-H), 8.78 (m, 2H, β-pyrrole-H13,17), 8.92 (m, 2H, β-pyrrole-H2,18), 9.46 (m, 2H, β-pyrrole-H3,12), 9.58 (m, 2H, β-pyrrole-H7,8); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 418 (5.09), 485 (4.00), 517 (3.91), 553 (3.64), 593 (3.66), 655 nm (4.23); HRMS [$C_{44}H_{46}N_4O$]: calcd 646.3671, found [M + 1] 647.3771.

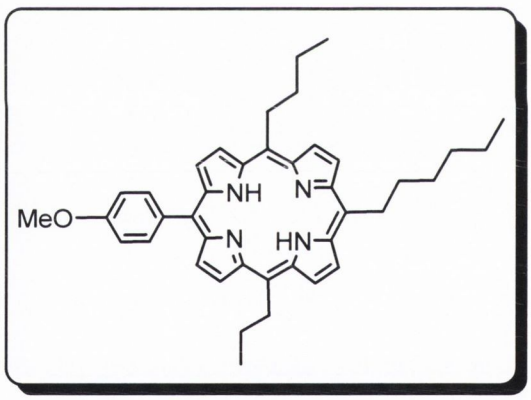
5-Butyl-10-hexyl-15-pentyl-20-(4-methoxyphenyl)porphyrin 177



n-Butyllithium (0.4 ml of 2.5 M solution in hexane, 1 mmol) was slowly added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-hexyl-15-(4-methoxyphenyl)porphyrin **170** (100 mg, 0.19 mmol) in 40 ml of dry THF at −80 °C under an argon atmosphere. After 15 min the solution was treated with 0.8 ml *n*-pentyl iodide (6.1 mmol) and stirred for 12 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 15, v/v) yielded the title compound (15 mg, 0.023 mmol, 13 %) as purple crystals, besides trisubstituted porphyrin (9 %) and starting material **170** (7 %); mp >300 °C; $R_f = 0.57$ (ethyl

acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.63 (s, 2H, N*H*), 0.87 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 1.37 (m, 5H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$), 1.56 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 1.86 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$), 2.56 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$), 4.13 (s, 3H, OCH_3), 5.02 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$), 7.33 (d, 2H, *J* = 8 Hz, Ph-H), 8.11 (d, 2H, *J* = 8 Hz, Ph-H), 8.85 (d, 2H, *J* = 5 Hz, β-pyrrole-H), 9.40 (d, 2H, *J* = 5 Hz, β-pyrrole-H), 9.52 (d, 2H, *J* = 5 Hz , β-pyrrole-H), 9.55 (d, 2H, *J* = 5 Hz, β-pyrrole-H); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 442 (5.09), 486 (3.51), 548 (3.27), 581 (3.51), 656 nm (4.27); HRMS [$C_{42}H_{50}N_4O$]: calcd 626.3984, found [M + 1] 627.4061.

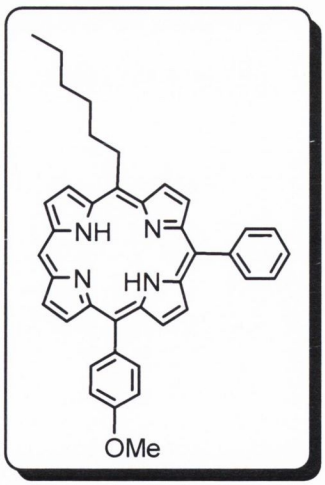
5-Butyl-10-hexyl-15-propyl-20-(4-methoxyphenyl)porphyrin 178



n-Butyllithium (0.4 ml of 2.5 M solution in hexane, 1 mmol) was slowly added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-hexyl-15-(4-methoxyphenyl)porphyrin **170** (100 mg, 0.19 mmol) in 40 ml of dry THF at −80 °C under an argon atmosphere. After 15 min the solution was treated with 0.7 ml *n*-propyl iodide (7.1 mmol) and stirred for 12 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification

was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 15, v/v) yielded the title compound (22 mg, 0.036 mmol, 18 %) as purple crystals, besides trisubstituted porphyrin (10 %) and starting material **170** (8 %); mp >300 °C; R_f = 0.62 (ethyl acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.63 (s, 2H, N*H*), 0.98 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$), 1.33-1.37 (m, 5H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$), 1.56 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.87 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$), 2.59 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$), 4.13 (s, 3H, OCH_3), 5.01 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$), 7.28 (d, 2H, *J* = 8 Hz, Ph-H), 8.09 (d, 2H, *J* = 8 Hz, Ph-H), 8.86 (d, 2H, *J* = 5 Hz, β-pyrrole-H), 9.42 (d, 2H, *J* = 5 Hz, β-pyrrole-H), 9.52-9.56 (m, 4H, β-pyrrole-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.79, 14.52, 22.36, 23.22, 28.49, 29.29, 29.91, 31.12, 31.52, 34.70, 35.37, 36.84, 38.45, 40.34, 50.97, 55.14, 111.61, 117.43, 118.25, 118.57, 118.80, 126.04, 128.38, 130.49, 134.55, 134.94, 158.79 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 418 (5.00), 487 (4.60), 517 (3.33), 555 (2.85), 598 (2.77), 655 nm (4.17); HRMS [$C_{40}H_{46}N_4O$]: calcd 598.3671, found [M + 1] 599.3739.

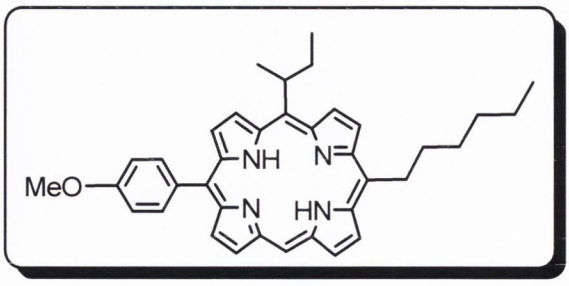
5-Hexyl-10-phenyl-15-(4-methoxyphenyl)porphyrin 181



Phenyllithium (0.8 ml of a 1.8 M solution in hexane, 0.02 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-hexyl-15-(4-methoxyphenyl)porphyrin **170** (100 mg, 0.19 mmol) in 40 ml of dry THF. The mixture was heated to 50 °C and stirred for 30 min. Subsequently, a mixture of 2 ml of water in 3 ml of

THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) yielded the title compound (51 mg, 0.088 mmol, 45 %) as purple crystals, besides starting material **170** (8 %); mp >300 °C; $R_f = 0.69$ (ethyl acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.87 (s, 2H, N*H*), 0.95 (t, 3H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.32 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$) 1.53 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.85 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.56 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.11 (s, 3H, OCH_3), 5.05 (t, 2H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.31 (d, 2H, *J* = 8 Hz, Ph-H), 7.82 (m, 3H, Ph-H), 8.16 (d, 2H, *J* = 8 Hz, Ph-H), 8.25 (m, 2H, Ph-H), 8.85-8.91 (2d, 2H, *J* = 5 Hz, β-pyrrole-H13,17), 8.96-9.03 (2d, 2H, *J* = 5 Hz, β-pyrrole-H8,12), 9.31-9.39 (2d, 2H, *J* = 5 Hz, β-pyrrole-H2,18), 9.51-9.61 (2d, 2H, *J* = 5 Hz, β-pyrrole-H3,7), 10.14 ppm (s, 1H, 20-meso-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.74 (10^6-C), 22.31 (10^5-C), 29.85 (10^4-C), 31.50 (10^3-C), 34.73 (10^2-C), 38.37 (10^1-C), 55.13 (C_{OCH3}), 103.82, 111.93, 118.26, 119.45, 119.61, 126.04, 127.03, 127.20, 127.93, 130.61, 130.75, 131.09, 131.37, 133.63, 134.01, 135.23, 142.43, 142.64, 158.93 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 441 (4.97), 548 (2.76), 596 (3.34), 644 nm (3.95); HRMS [$C_{39}H_{36}N_4O$]: calcd 576.2889, found [M + 1] 577.2946.

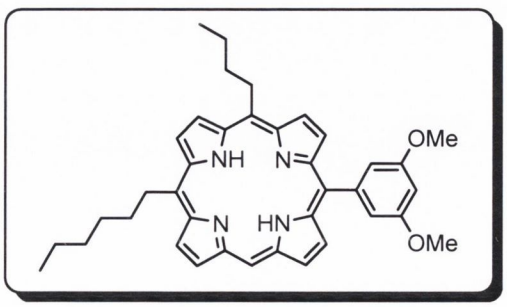
5-(*sec*-Butyl)-10-hexyl-20-(4-methoxyphenyl)porphyrin 182



sec-Butyllithium (1 ml of a 2.5 M solution in hexane, 2.5 mmol) was added under an argon atmosphere to a 50 ml Schlenk flask charged with a solution of 5-hexyl-15-(4-methoxyphenyl)porphyrin **170** (100 mg, 0.19 mmol) in 30 ml of dry THF at −80 °C. The

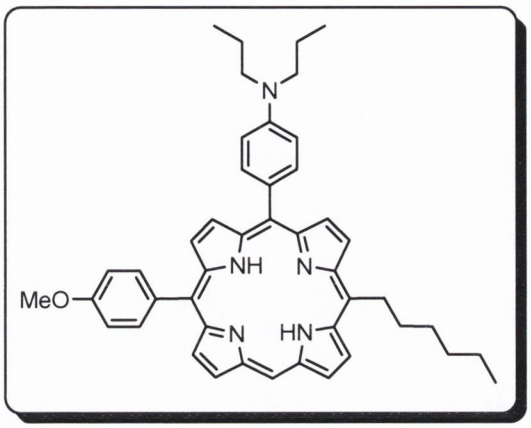
mixture changed from deep purple to brown within 30 min. The mixture was heated to 50 °C and stirred for 30 min. Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) yielded the title compound (15 mg, 0.026 mmol, 14 %) as purple crystals, besides starting material **170** (10 %); mp >300 °C; R_f = 0.62 (ethyl acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.92 (s, 2H, N*H*), 0.89 (t, 3H, *J* = 7.6, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.10 (t, 3H *J* = 7.6 Hz, $CH(CH_3)(CH_2CH_3)$), 1.42 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.57 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.89 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.46 (d, 3H, *J* = 7.4 Hz, $CH(CH_3)(CH_2CH_3)$), 2.60 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.02 (m, 2H, $CH(CH_3)(CH_2CH_3)$), 4.13 (s, 3H, OCH_3), 5.03 (t, 2H, *J* = 7.6 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 5.46 (m, 1H, $CH(CH_3)(CH_2CH_3)$), 7.33 (d, 2H, *J* = 8 Hz, Ph-H), 8.12 (d, 2H, *J* = 8 Hz, Ph-H), 8.93 (d, 2H, *J* = 5 Hz, β-pyrrole-H2,18), 9.23-9.33 (2d, 2H, *J* = 5 Hz, β-pyrrole-H13,17), 9.58 (2d, 2H, *J* = 5 Hz, β-pyrrole-H8,12), 9.66-9.78 (2d, 2H, *J* = 5 Hz, β-pyrrole-H3,7), 10.01 ppm (s, 1H, 15-meso-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.75, 13.83, 22.35, 27.02, 29.28, 31.51, 35.18, 35.49, 38.43, 42.60, 55.15, 102.96, 111.74, 117.56, 118.88, 124.84, 135.06, 158.87 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 440 (4.96), 486 (3.61), 585 (3.63), 656 nm (3.94); HRMS [$C_{37}H_{40}N_4O$]: calcd 556.3202, found [M + 1] 557.3257.

5-Butyl-10-(3,5-dimethoxyphenyl)-20-hexylporphyrin 185



n-Butyllithium (0.4 ml of 2.5 M solution in hexane, 1 mmol) was slowly added (ca. 1 h) under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of 5-hexyl-15-(3,5-dimethoxyphenyl)porphyrin **172** (100 mg, 0.18 mmol) in 40 ml of dry THF. The mixture was heated to 50 °C and stirred for 30 min. Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.06 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) yielded the title compound (16 mg, 0.027 mmol, 15 %) as purple crystals, besides starting material **172** (12 %); mp >300 °C; R_f = 0.60 (ethyl acetate/*n*-hexane, 1 : 5, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ= −2.91 (s, 2H, N*H*), 0.93 (t, 3H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.16 (t, 3H, *J* = 7.5 $CH_2CH_2CH_2CH_3$), 1.26 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.47 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.88 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 2.54 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.00 (s, 6H, OCH_3), 5.04 (t, 4H, *J* = 7.8 Hz, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 6.94 (m, 1H, Ph-H), 7.42 (m, 2H, Ph-H), 9.03 (2d, 2H, *J* = 5 Hz, β-pyrrole-H8,12), 9.23-9.34 (2d, 2H, *J* = 5 Hz, β-pyrrole-H13,17), 9.52-9.65 (m, 4H, β-pyrrole-H2,3,7,18), 10.14 ppm (s, 1H, 15-meso-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.74, 13.80, 22.33, 25.17, 29.27, 29.89, 30.51, 31.50, 38.40, 40.70, 55.19, 99.51, 103.07, 117.31, 120.08, 127.71, 130.45, 143.45, 158.47 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 436 (5.02), 486 (3.11), 544 (2.86), 581 (3.50), 656 nm (3.72); HRMS [$C_{38}H_{42}N_4O_2$]: calcd 586.3307, found [M + 1] 587.3389.

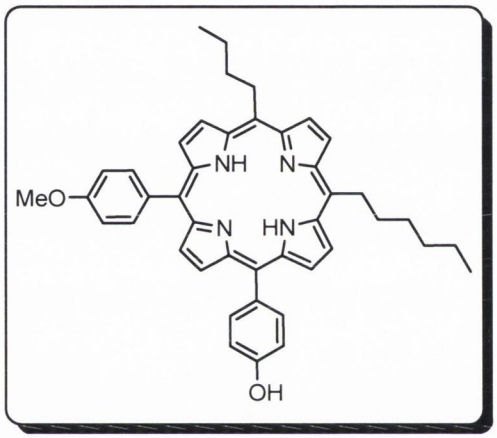
5-[*p*-(Dipropylamino)phenyl]-10-hexyl-20-(4-methoxyphenyl)porphyrin 190



n-Butyllithium (2 ml of a 2.5 M solution in hexane, 5 mmol) was added under an argon atmosphere to a 100 ml Schlenk flask charged with a solution of *p*-bromoaniline (0.5 g, 2.5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for another 2 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5-hexyl-15-(4-methoxyphenyl)porphyrin **170** (100 mg, 0.19 mmol) in 40 ml of dry THF under an argon atmosphere at −80 °C . The mixture changed from deep purple to brown within 30 min. After 1 h the solution was treated with 1 ml propyl iodide (10 mmol) and stirring for 12 h and heating to 70 °C (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 10, v/v) yielded the title compound (41 mg, 0.06 mmol, 31 %) as purple crystals, besides starting material **170** (13 %); mp >300 °C; R_f = 0.54 (ethyl acetate/*n*-hexane, 1 : 8, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.81 (s, 2H, N*H*), 0.92 (t, 3H, *J* = 7.2 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.13 (m, 6H, $N(CH_2CH_2CH_3)_2$), 1.27 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.57 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.83-1.94 (m, 6H, $CH_2CH_2CH_2CH_2CH_2CH_3$, $N(CH_2CH_2CH_3)_2$), 2.61 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.54 (m, 4H, $N(CH_2CH_2CH_3)_2$), 4.12 (s, 3H, OCH_3), 5.04 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.05 (d, 2H, *J* = 7.5 Hz, Ph-H), 7.34 (d, 2H, *J* = 7.5

Hz, Ph-H), 8.05 (d, 2H, J = 7.5 Hz, Ph-H), 8.15 (d, 2H, J = 7.5 Hz, Ph-H), 8.88-9.01 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 9.02-9.13 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 9.28-9.37 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 9.51-9.61 (d, 2H, J = 5.0 Hz, β-pyrrole-H), 10.09 ppm (s, 1H, 15-meso-H); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 443 (5.09), 486 (3.81), 585 (3.67), 656nm (4.22); HRMS [$C_{45}H_{49}N_5O$]: calcd 675.3937, found [M + 1] 676.4039.

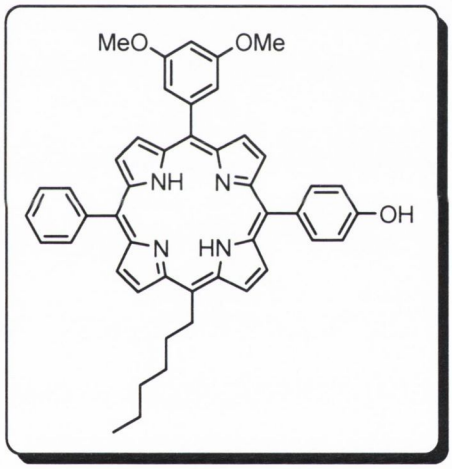
5-Butyl-10-hexyl-15-(4-hydroxyphenyl)-20-(4-methoxyphenyl)porphyrin 193



n-Butyllithium (2 ml of a 2.5 M solution in hexane, 10 mmol) was added under an argon atmosphere to a 50 ml Schlenk flask charged with a solution of *p*-bromophenol (0.43 g, 2.5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 18 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5-butyl-10-hexyl-20-(4-methoxyphenyl)porphyrin **192** (40 mg, 0.07 mmol) in 30 ml of dry THF under an argon atmosphere. Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 8, v/v) yielded the title compound (28 mg, 0.04 mmol, 60 %) as purple crystals, besides starting material **192** (8 %); mp >300 °C; R_f = 0.52 (ethyl acetate/*n*-hexane, 1 : 2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.66 (s, 2H, N*H*), 0.95 (t, 3H, J = 7.5 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.15 (t, 3H, J = 7.5 Hz, $CH_2CH_2CH_2CH_2CH_3$), 1.29 (m, 2H,

$CH_2CH_2CH_2CH_2CH_2CH_3$), 1.53 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.89 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.57 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.11 (s, 3H, OCH_3), 5.01 (t, 4H, J = 7.8 Hz, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.15 (d, 2H, J = 7.5 Hz, Ph-H), 7.30 (d, 2H, J = 7.5 Hz, Ph-H), 8.04 (d, 2H, J=7.5 Hz, Ph-H), 8.11 (d, 2H, J = 7.5 Hz, Ph-H),, 8.78 (s, 2H, β-pyrrole-H17,18), 8.97 (2d, 2H, J = 5 Hz, β-pyrrole-H2,13), 9.45 (2d, 2H, J = 5 Hz, β-pyrrole-H3,12), 9.59 (s, 2H, β-pyrrole-H7,8); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 446 (5.08), 486 (3.36), 581 (3.15), 615 (3.39), 656 nm (4.24); HRMS [$C_{43}H_{44}N_4O_2$]: calcd 648.3464, found [M + 1] 649.3548.

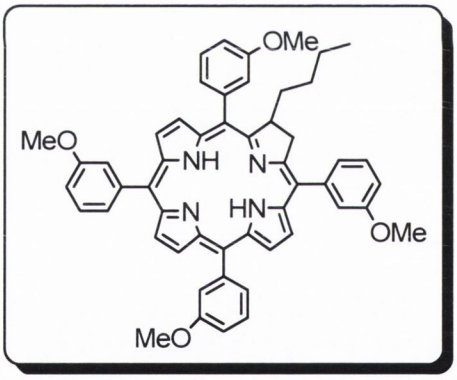
5-(3,5-dimethoxypheny)-10-(4-hydroxyphenyl)-15-hexyl-20-phenyl-porphyrin 195



n-Butyllithium (2 ml of a 2.5 M solution in hexane, 10 mmol) was added under an argon atmosphere to a 50 ml Schlenk flask charged with a solution of *p*-bromophenol (0.43 g, 2.5 mmol) in 10 ml of dry diethyl ether at 0 °C. After addition of *n*-butyl lithium the cold bath was removed and stirring was continued for 18 h at room temperature. To the vigorously stirred mixture was added rapidly a solution of 5-(3,5-dimethoxyphenyl)-10-phenyl-15-hexylporphyrin **194** (40 mg, 0.07 mmol) in 30 ml of dry THF under an argon atmosphere. Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic

solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 5, v/v) yielded the title compound (17 mg, 0.024 mmol, 37 %) as purple crystals, besides starting material **194** (10 %); mp >300 °C; R_f = 0.28 (ethyl acetate/*n*-hexane, 1 : 1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = −2.74 (s, 2H, N*H*), 0.92 (t, 3H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.41 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$) 1.53 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.84 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.59 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.97 (s, 6H, OCH_3), 5.04 (t, 2H, *J* = 8.1 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 6.77 (m, 4H, Ph-H), 7.22-7.39 (m, 4H, Ph-H), 7.79 (m, 2H, Ph-H), 8.07 (d, 1H, *J* = 8 Hz, Ph-H), 8.21 (d, 1H, *J* = 6.4 Hz, Ph-H), 8.79-8.83 (2d, 2H, *J* = 5 Hz, β-pyrrole-H3,7), 8.90-8.97 (m, 4H, β-pyrrole-H2,8,12,18), 9.50 (d, 2H, *J* = 5 Hz, β-pyrrole-H13,17); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 449 (4.04), 514 (3.66), 552 (3.60), 585 (3.60), 656 nm (4.34); HRMS [$C_{46}H_{42}N_4O_3$]: calcd 698.3256, found [M + 1] 699.3335.

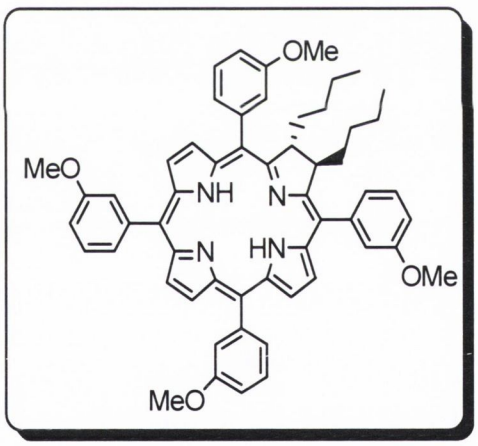
7-Butyl-5,10,15,20-tetrakis(3-methoxyphenyl)chlorin 202



5,10,15,20-Tetrakis(3-methoxyphenyl)porphyrin **200** (100 mg, 0.13 mmol) was dissolved in dry THF (30 ml) and cooled to −80 °C under an argon atmosphere. *n*-Butyllithium (0.3 ml of 2.5 M solution in hexane, 0.75 mmol) was added and the mixture warmed to R.T. and stirred for 3 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 6, v/v). The first fraction

consisted of **202** (18 mg, 0.022 mmol, 17 %) and the second fraction of **203** (16 mg, 0.018 mmol, 14 %). **202:** mp = 233 °C; R_f = 0.70 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.61 (t, 3H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_3$), 1.06 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.66 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.88 (m, 2H, $CH_2CH_2CH_2CH_3$), 3.22 (dd, 1H, ^3J(H,H) = 6 Hz, ^2J=14 Hz, 3-H *syn*), 4.03 (m, 12H, OCH_3), 4.50 (dd, 1H, ^3J(H,H,) = 9 Hz, ^2J = 14 Hz, 3-H *anti*), 4.78 (m, 1H; 2-H), 6.54-7.90 (m, 16H, Ph-H), 8.31 (m, 2H, β-pyrrole-H), 8.51 (s, 2H, β-pyrrole-H), 8.66 (m, 2H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 5.21, 14.17, 26.00, 34.22, 45.42, 55.90, 68.39, 112.86, 117.50, 132.67, 155.18; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 421 (5.19), 486 (3.80), 519 (4.09), 547 (3.94), 598 (3.75), 656 nm (4.39); MS (EI, 80 eV): *m/z* (%): 792 (100) [M^+], 735 (51) [$M^+ - C_4H_9$]; HRMS [$C_{52}H_{48}N_4O_4$]: calcd 792.3675, found [M + 1] 793.3747.

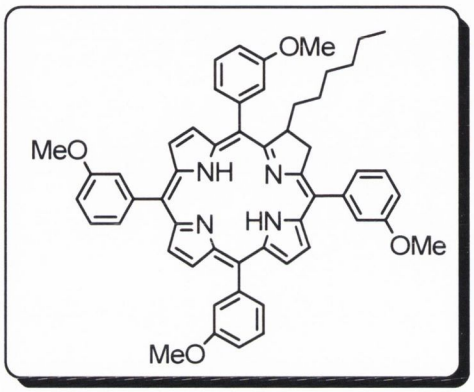
trans-7,8-Dibutyl-5,10,15,20-tetrakis(3-methoxyphenyl)chlorin 203



Mp = 245, °C; R_f=0.56 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −1.44 (s, 2H, N*H*), 0.80 (t, 6H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_3$), 0.95-1.32 (m, 8H, $CH_2CH_2CH_2CH_3$), 1.60, 1.75 (m, 4H, $CH_2CH_2CH_2CH_3$), 4.00 (m, 12H, OCH_3), 4.42 (dd, 2H, ^3J(H,H,) = 9 Hz, 2-, 3-H), 7.20-7.92 (m, 16H, Ph-H), 8.24 (m, 2H, β-pyrrole-H), 8.50 (s, 2H, β-pyrrole-H), 8.65 ppm (m, 2H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 6.32, 13.49, 22.08, 28.22, 30.99, 54.99, 112.65, 119.52, 126.51, 127.05, 143.27, 158.04 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 420 (5.19), 454 (4.17), 519 (4.08), 519 (4.08), 547 (3.93), 652 nm (4.32); MS (EI, 80 eV): *m/z* (%): 848 (14) [M^+], 818 (100) [$M^+ - 2(CH_3)$], 792 (80) [$M^+ - C_4H_9$

+ H], 735 (56) [M^+ − 2(C_4H_9) + H], 611 (16) [M^+ − 2(C_4H_9) + H − 4(OCH_3)]; HRMS [$C_{56}H_{56}N_4O_4$]: calcd 848.4301, found [M + 1] 849.5168.

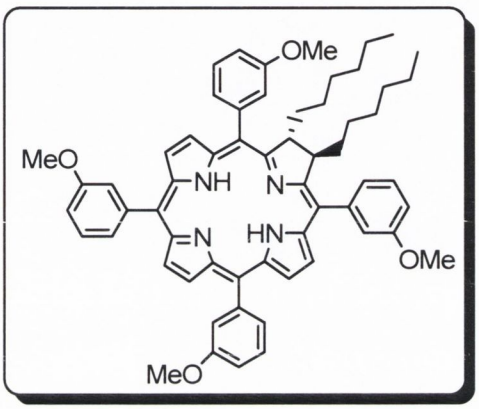
7-Hexyl-5,10,15,20-tetrakis(3-methoxyphenyl)chlorin 204



5,10,15,20-Tetrakis(3-methoxyphenyl)porphyrin **200** (100 mg, 0.13 mmol) was dissolved in dry THF (30 ml) and cooled to − 80 °C under an argon atmosphere. *n*-Hexyllithium (0.6 ml of 2.5 M solution in hexane, 1.2 mmol) was added and the mixture warmed to R.T. and stirred for 3 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 6, v/v). The first fraction consisted **204** (24 mg, 0.029 mmol, 22 %) and the second fraction of **205** (25 mg, 0.027 mmol, 20 %). **204:** mp = 220 °C; R_f = 0.76 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −1.46 (s, 2H, N*H*), 0.75 (t, 3H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.03 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.08 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.40 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.86 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.75 (dd, 1H, ^3J(H,H) = 6 Hz, ^2J = 14 Hz, 3-H *syn*), 3.97 (m, 12H, OCH_3), 4.40 (dd, 1H, ^3J(H,H) = 9 Hz, ^2J = 14 Hz, 3-H *anti*), 4.74 (m, 1H; 2-H), 7.25-7.85 (m, 16H, Ph-H), 8.26 (m, 2H, β-pyrrole-H), 8.47 (s, 2H, β-pyrrole-H), 8.64 (m, 2H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 4.66, 14.29, 22.85, 30.94, 36.85, 46.91, 50.08, 55.87, 71.11,

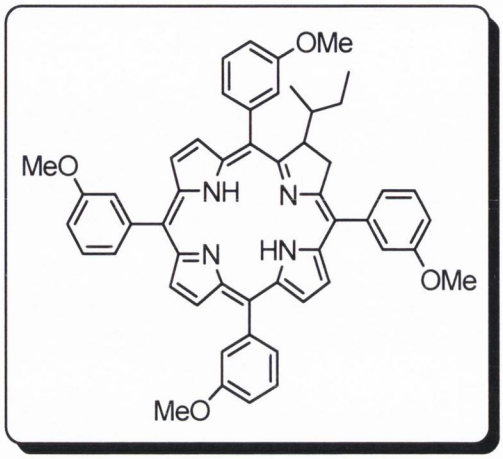
108.43, 118.55, 140.64, 143.60, 154.62; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 451 (5.18), 557 (3.59), 605 (3.89), 656 nm (4.44); MS (EI, 80 eV): *m/z* (%): 820 (100) [M^+], 735 (51) [$M^+ - C_6H_{13}$]; HRMS [$C_{54}H_{52}N_4O_4$]: calcd 820.3988, found [M + 1] 821.4045.

trans-7,8-Dihexyl-5,10,15,20-tetrakis(3-methoxyphenyl)chlorin 205



Mp = 242 °C; R_f =0.71 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −1.44 (s, 2H, N*H*), 0.65 (t, 6H, *J* = 8 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.06-1.26 (m, 8H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.54 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.94 (m, 4H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.19 (t, 4H, *J* = 8 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 3.97 (m, 12H, OCH_3), 4.38 (2d, 2H, ^3J(H,H,) = 9 Hz, 2-, 3-H), 7.20-7.82 (m, 16H, Ph-H), 8.22 (m, 2H, β-pyrrole-H), 8.46 (s, 2H, β-pyrrole-H), 8.61 ppm (m, 2H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 5.18, 14.21, 22.53, 29.20, 34.22, 52.36, 55.84, 73.32, 120.10, 126.05, 127.88, 128.97, 141.46, 144.00, 154.46 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 448 (5.25), 556 (3.74), 606 (3.98), 652 nm (4.53); MS (EI, 80 eV): *m/z* (%): 903 (34) [M^+ − H], 847 (100) [$M^+ - C_4H_9$], 818 (22) [$M^+ - C_6H_{13}$ − H], 791 (40) [$M^+ - 2(C_4H_9)$ + H], 733 (13) [$M^+ - 2(C_6H_{13})$ − H]; HRMS [$C_{60}H_{64}N_4O_4$]: calcd 904.4927, found [M + 1] 905.5029.

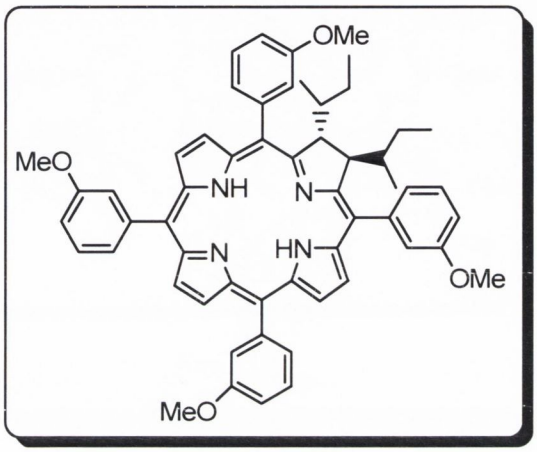
7-(*sec*-Butyl)-5,10,15,20-tetrakis(3-methoxyphenyl)chlorin 206



5,10,15,20-Tetrakis(3-methoxyphenyl)porphyrin **200** (100 mg, 0.13 mmol) was dissolved in dry THF (30 ml) and cooled to − 80 °C under an argon atmosphere. *sec*-Butyllithium (0.3 ml of 2.5 M solution in hexane, 0.75 mmol) was added and the mixture warmed to R.T. and stirred for 3 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 6, v/v). The first fraction consisted **206** (27 mg, 0.034 mmol, 25 %) and the second fraction of **207** (20 mg, 0.023 mmol, 18 %). **206:** mp = 228 °C; R_f = 0.66 (ethyl acetate/*n*-hexane, 1 : 3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −1.47 (s, 2H, N*H*), 0.65 (t, 3H, *J* = 9 Hz, $CH(CH_3)(CH_2CH_3)$), 0.87 (d, 3H, *J* = 8 Hz, $CH(CH_3)(CH_2CH_3)$), 1.27 (m, 2H, $CH(CH_3)(CH_2CH_3)$), 1.94 (m, 1H, $CH(CH_3)(CH_2CH_3)$), 3.19 (dd, 1H, ^3J(H,H) = 6 Hz, ^2J = 14 Hz, 3-H *syn*), 4.01 (m, 12H, OCH_3), 4.22 (dd, 1H, ^3J(H,H,) = 9 Hz, ^2J = 14 Hz, 3-H *anti*), 4.98 (m, 1H; 2-H), 7.22−7.69 (m, 16H, Ph-H), 8.24 (m, 2H, β-pyrrole-H), 8.48 (s, 2H, β-pyrrole-H), 8.65 ppm (m, 2H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 5.18, 12.20, 26.57, 34.22, 48.08, 55.85, 60.94, 113.95, 123.73, 128.30, 136.29, 155.27, 160.13 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 449 (5.16), 556 (3.57), 559 (3.88), 656 nm (4.43); MS (EI, 80

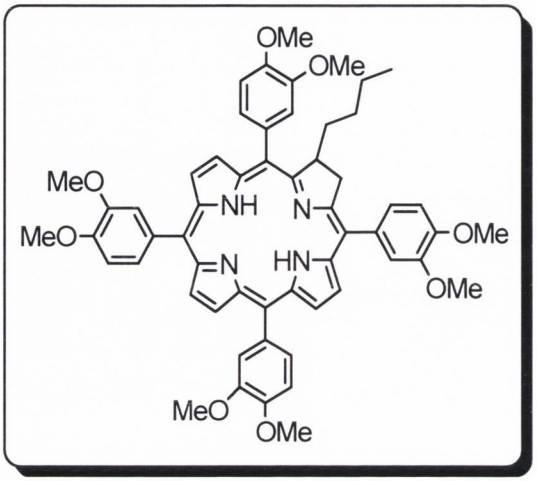
eV): *m/z* (%): 792 (28) [M^+], 735 (10) [$M^+ - C_4H_9$]; HRMS [$C_{52}H_{48}N_4O_4$]: calcd 792.3675, found [M + 1] 793.3729.

trans-7,8-Di(*sec*-butyl)-5,10,15,20-tetrakis(3-methoxyphenyl)chlorin 207



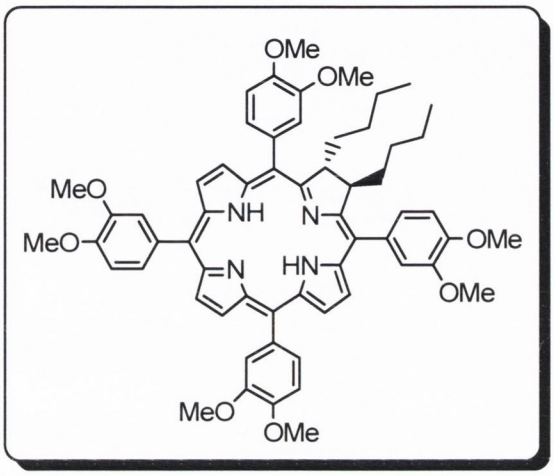
Mp = 245 °C; R_f = 0.59 (ethyl acetate/*n*-hexane, 1 : 3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −1.50 (s, 2H, N*H*), 0.66 (t, 6H, *J* = 8 Hz, $CH(CH_3)(CH_2CH_3)$), 0.94 (m, 6H, $CH(CH_3)(CH_2CH_3)$), 1.27 (m, 4H, $CH(CH_3)(CH_2CH_3)$), 1.99 (m, 2H, $CH(CH_3)(CH_2CH_3)$), 3.90 (m, 12H, OCH_3), 4.53 (m, 2H, 2-, 3-H), 7.20–7.90 (m, 16H, Ph-H), 8.27 (m, 2H, β-pyrrole-H), 8.48 (s, 2H, β-pyrrole-H), 8.62 ppm (m, 2H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 5.14, 12.33, 23.81, 32.70, 43.92, 55.85, 67.41, 100.44, 111.34, 113.84, 135.71, 141.68, 145.22, 152.63, 158.91 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 446 (5.16), 552 (4.07), 595 (4.13), 656 nm (4.47); MS (EI, 80 eV): *m/z* (%): 847 (92) [M^+ − H], 791 (100) [$M^+ - C_4H_9$], 734 (68) [$M^+ - 2(C_4H_9)$], 424 (17) [M^{++}]; HRMS [$C_{56}H_{56}N_4O_4$]: calcd 848.4301, found [M + 1] 849.4402.

7-Butyl-5,10,15,20-tetrakis(3,4-dimethoxyphenyl)chlorin 208



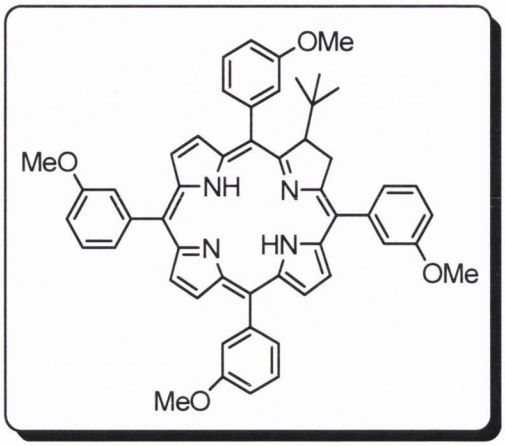
5,10,15,20-Tetrakis(3,4-dimethoxyphenyl)porphyrin **201** (100 mg, 0.13 mmol) was dissolved in dry THF (30 ml) and cooled to − 80 °C under an argon atmosphere. *n*-Butyllithium (0.3 ml of 2.5 M solution in hexane, 0.75 mmol) was added and the mixture warmed to R.T. and stirred for 3 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 6, v/v). The first fraction consisted **208** (9 mg, 0.01 mmol, 9 %) and the second fraction of **209** (8 mg, 0.008 mmol, 7 %). **208:** mp = 233 °C; R_f= 0.80 (ethyl acetate/*n*-hexane, 1 : 8, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −1.41 (s, 2H, N*H*), 0.58 (t, 3H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_3$), 1.20 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.65 (m, 2H, $CH_2CH_2CH_2CH_3$), 2.20 (m, 2H, $CH_2CH_2CH_2CH_3$), 2.85 (m, 1H, 3-H*syn*), 3.82-4.21 (m, 24H, OCH_3), 4.38 (m, 1H, 3-H*anti*), 4.71 (m, 1H, 2-H), 7.02-7.66 (m, 12H, Ph-H), 8.30 (2d, 2H, β-pyrrole-H3,12), 8.50 (s, 2H, β-pyrrole-H17,18), 8.65 ppm (m, 2H, β-pyrrole-H2,13); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 425 (5.20), 485 (4.37), 523 (4.26), 551 (4.21), 593 (4.10), 655 nm (4.64); HRMS [$C_{56}H_{56}N_4O_8$]: calcd 912.4098, found [M + 1] 913.4211.

trans-7,8-Dibutyl-5,10,15,20-tetrakis(3,4-dimethoxyphenyl)chlorin 209



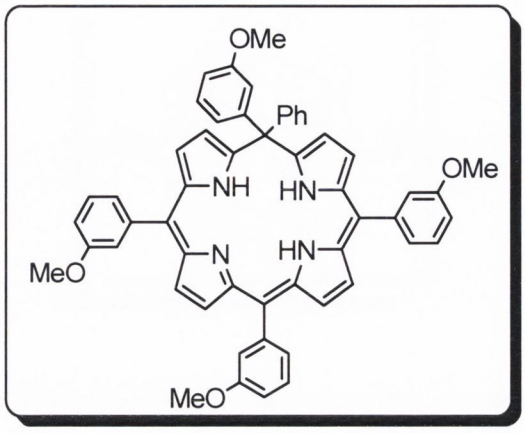
Mp = 247 °C; R_f = 0.70 (ethyl acetate/*n*-hexane, 1 : 8, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = −1.43 (s, 2H, N*H*), 0.97 (t, 6H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_3$), 1.10-1.40 (m, 8H, $CH_2CH_2CH_2CH_3$), 1.60, 2.03 (m, 4H, $CH_2CH_2CH_2CH_3$), 4.04-4.21 (m, 24H, OCH_3), 4.72 (m, 2H, 2-, 3-H), 6.92-7.80 (m, 12H, Ph-H), 8.27 (m, 2H, β-pyrrole-H3,12), 8.51 (s, 2H, β-pyrrole-H17,18), 8.66 ppm (m, 2H, β-pyrrole-H2,13); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 4.60 (5.14), 556 (3.86), 598 (4.04), 656 nm (4.46); HRMS [$C_{60}H_{64}N_4O_8$]: calcd 968.4724, found [M + 1] 969.4019.

7-(*tert*-Butyl)-5,10,15,20-tetrakis(3-methoxyphenyl)chlorin 210



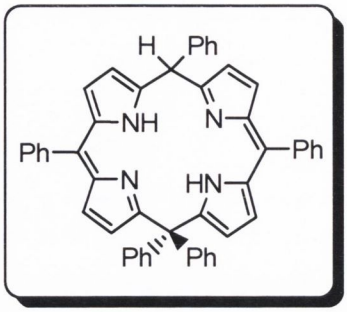
5,10,15,20-Tetrakis(3-methoxyphenyl)porphyrin **200** (100 mg, 0.13 mmol) was dissolved in dry THF (30 ml) and cooled to − 80 °C under an argon atmosphere. *t*-Butyllithium (0.3 ml of 2.5 M solution in hexane, 0.75 mmol) was added and the mixture warmed to R.T. and stirred for 3 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 6, v/v) yielded the title compound (32 mg, 0.04 mmol, 30 %); mp = 221 °C; R_f = 0.55 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = − 1.08 (s, 2H, N*H*), δ = 0.40 (s, 9H, C(C*H*$_3$)$_3$), 3.83 (dd, ^3J(H,H) = 6 Hz, ^2J = 14 Hz, 1H; 3-H *syn*), 3.99 (m, 12H, OCH_3), 4.46 (dd, ^3J(H,H,) = 9 Hz, ^2J = 14 Hz, 1H; 3-H *anti*), 4.66 (m, 1H, 2-H), 7.26-8.00 (m, 16H, Ph-H), 8.28 (m, 2H, β-pyrrole-H), 8.47 (s, 2H, β-pyrrole-H), 8.62 ppm (m, 2H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 5.21,27.90, 34.22, 37.52, 55.93, 112.74, 117.49, 127.95, 132.61, 155.23 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 418 (5.12), 486 (4.41), 581 (4.01), 656 nm (4.18); MS (EI, 80 eV): *m/z* (%): 792 (6) [M^+], 735 (17) [$M^+ - C(CH_3)_3$]; HRMS [$C_{52}H_{48}N_4O_4$]: calcd 792.3675, found [M + 1] 793.3736.

22-Hydro-5,10,15,20-tetrakis(3-methoxyphenyl)-5-phenylporphyrin 211



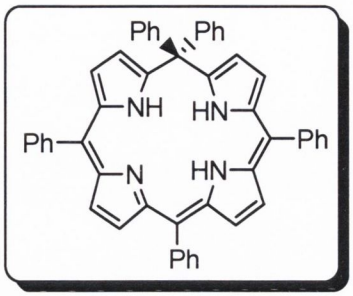
5,10,15,20-Tetrakis(3-methoxyphenyl)porphyrin **200** (100 mg, 0.13 mmol) was dissolved in dry THF (30 ml) under an argon atmosphere. Phenyllithium (1 ml of a 1.8 M solution in hexane, 0.03 mmol) was added and the mixture heated at 70 °C for 1 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 7, v/v) yielded the title compound (22 mg, 0.027 mmol, 20 %); Mp = 232 °C; R_f = 0.77 (ethyl acetate/*n*-hexane, 1 : 4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 3.80 (m, 12H, OCH_3), 5.51 (m, 2H, β-pyrrole-H), 6.08 (s, 2H, β-pyrrole-H), 6.02 (m, 2H, β-pyrrole-H), 6.64 (m, 2H, β-pyrrole-H), 6.80-7.62 (m, 21H, Ph-H), 10.5 (s, 3H, N*H*); UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 355 (5.17), 486 (4.73), 532 (5.00), 567 (5.03), 656 nm (4.19); MS (EI, 80 eV): *m/z* (%): 812 (28) [M^+], 811 (72) [M^+ −H], 781 (100) [$M^+ - OCH_3$], 704 (11) [$M^+ - C_6H_5 - OCH_3$].

5-Hydro-5,10,15,15`,20-pentaphenylporphyrin 212



5,10,15,20-tetraphenylporphyrin **199** (100 mg, 0.13 mmol) was dissolved in dry THF (30 ml) and under an argon atmosphere. Phenyllithium (1 ml of a 1.8 M solution in hexane, 0.03 mmol) was added and the mixture refluxed 70 °C for 1 h (TLC control). Subsequently, a mixture of 2 ml of water in 3 ml of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF (0.03 M) was added and the reaction mixture was stirred for another 60 min at room temperature. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed under vacuum. Final purification was achieved by column chromatography and elution with ethyl acetate/*n*-hexane (1 : 6, v/v). The first fraction consisted **212** (17 mg, 0.024 mmol, 15 %) and the second fraction of **213** (51 mg, 0.07 mmol, 45 %). **212:** Mp = 234 °C; R_f = 0.16 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 3.10 (s, 1H, 5-H), 5.80 (d, 2H, *J* = 4.5 Hz, β-pyrrole-H), 6.20 (d, 2H, *J*= 4.5 Hz, β-pyrrole-H), 6.25 (d, 2H, *J* = 4.5 Hz, β-pyrrole-H), 6.30 (d, 2H, *J*= 4.5 Hz, β-pyrrole-H), 6.95−7.60 (m, 25H, Ph-H), 10.5 (s, 2H, N*H*) ppm; ^{13}C NMR (60 MHz, $CDCl_3$): δ = 58.20, 75.55, 125.22, 127.95, 128.44, 129,45, 130.62, 131.50, 133.78, 135.00, 138.25, 140.33, 141.66, 144.38, 146.00, 165.25 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 325 (5.15), 440 (5.09), 500 (4.97), 660 nm (4.57); MS (EI, 80 eV): *m/z* (%): 692 (7) [M^+], 691 (9) [M^+ −H], 614 (20) [$M^+ - C_6H_5 - H$], 346 (8) [M^{++}].

22-Hydro-5,5`,10,15,20-pentaphenylporphyrin 213



Mp = 215 °C; R_f = 0.16 (ethyl acetate/*n*-hexane, 1 : 6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 5.50 (s, 2H, β-pyrrole-H), 6.05 (s, 2H, β-pyrrole-H), 6.15 (d, 2H, *J* = 4.5 Hz, β-pyrrole-H), 6.60 (d, 2H, *J*= 4.5 Hz, β-pyrrole-H), 7.10-7.60 (m, 25H, Ph-H), 10.55, 12.6 ppm (each s, 3H, N*H*); ^{13}C NMR (60 MHz, $CDCl_3$): δ = 56.50, 110.00, 123.22, 127.57, 128.46, 129,38, 130.58, 131.58, 134.70, 135.46, 138.47, 140.33, 141.66, 144.38, 145.00, 152.25, 179.00 ppm; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 350 (5.14), 430 (4.98), 510 (4.74), 550 (4.91), 660 nm (4.44); MS (EI, 80 eV): *m/z* (%): 692 (20) [M^+], 691 (50) [M^+ –H], 614 (28) [M^+ – C_6H_5 – H], 346 (18) [M^{++}].

References

1. E. Hückel, *Z. Phys.* **1931**, *70*, 204–286.
2. M.K. Cyranski, T.M. Krygowski, M. Wisiorowski, N. J. R. van Eikema Hommes, P. V. Ragué Schleyer, *Angew. Chem.* **1998**, *110*, 187; *Angew. Chem. Int. Ed.* **1998**, *37*, 177–180.
3. (a) K. J. Thurlow, The International Union of Pure and Applied Chem. (IUPAC) for nomenclature part 2, organic, inorganic and others. *Chemical Nomenclature* **1998**, 127–145. (b) K.M. Smith (Ed.), in *Porphyrins and Metalloporphyrins*, Elsevier, Amsterdam, **1975**, pp 3.
4. (a) M. O. Senge in *The Porphyrin Handbook*; ed by K. M. Smith and R. Guilard, Academic Press, New York, **2000**, *Vol. 1*, pp. 239–347. (b) Floriani, Carlo; Floriani-Moro in *The Porphyrin Handbook*; ed by K. M. Kadish, K. M. Smith, and R. Guilard. **2000**, *Vol. 3*, 405–420. (c) R. Paolesse, S. Nardis, F. Sagone, R. G. Khoury, *J. Org. Chem.* **2001,** *66*, 550–556.
5. R. B. Woodward, *Ind. Chim. Belge* **1962**, *11*, 1293–1308.
6. J. H. Fuhrhop, J. Subramanian, *Philo. Trans. R. Soc. London*, Series B: Biological Sciences **1976**, *273*, 335–352.
7. P. Rothemund, *J. Am. Chem. Soc.* **1935**, *57*, 2010–2011.
8. P. Rothemund, *J. Am. Chem. Soc.* **1936**, *58*, 625–627.
9. P. Rothemund, *J. Am. Chem. Soc.* **1939**, *61*, 2912–2915.
10. R. H. Ball, G. D. Dorough, M. Calvin, *J. Am. Chem. Soc.* **1946**, *68*, 2278–2281.
11. D. W. Thomas, A. E. Martell, *J. Am. Chem. Soc.* **1956**, *78*, 1335–1338.
12. E. B. Fleischer, *Inorg. Chem.* **1962**, *1*, 493–495.
13. N. Datta-Gupta, T. J. Bardos, *J. Heterocycl. Chem.* **1966**, *3*, 495–502.
14. A. D. Adler, F. R. Longo, W. Shergalis, *J. Am. Chem. Soc.* **1964**, *86*, 3145–3149.
15. A. D. Adler, F. R. Longo, J. D. Finarelli, J. Goldmacher, J. Assour, L. Korsakoff, *J. Org. Chem.* **1967**, *32*, 476–476.
16. A. D. Adler, F. R. Longo, J. D. Finarelli, M. G. Finarelli, *J. Heterocycl. Chem.* **1968**, *5*, 669–678.
17. S. S. Eaton, G. R. Eaton, *J. Am. Chem. Soc.* **1975**, *97*, 3660–3666.
18. S. S. Eaton, G. R. Eaton, R. H. Holm, *J. Organomet. Chem.* **1972**, *39*, 179–195.
19. R. G. Little, *J. Heterocycl. Chem.* **1981**, *18*, 129–133.

20. A. Shirazi, H. M. Goff, *J. Am. Chem. Soc.* **1982**, *104*, 6318–6322.
21. J. Winkelman, G. Slater, J. Grossman, *Cancer Res.* **1967**, *27*, 2060–2064.
22. L. Barloy, D. Dolphin, D. Dupre, T. P. Wijesekera, *J. Org. Chem.* **1994**, *59*, 7976–7985.
23. L. R. Milgrom, P.J. F. Dempsey, G. Yahioglu, *Tetrahedron* **1996**, *52*, 9877–9890.
24. R. G. Little, J. A. Anton, P. A. Loach, J. A. Ibers, *J. Heterocycl. Chem.* **1975**, *12*, 343–349.
25. J. L. Y. Kong, P. A. Loach, *J. Heterocycl. Chem.* **1980**, *17*, 737–744.
26. S. Raines, C. A. Kovacs, *J. Heterocycl. Chem.* **1970**, *7*, 223–225.
27. W. Herz, K. Dittmer, S. J. Cristol, *J. Am. Chem. Soc.* **1947**, *69*, 1698–1700.
28. H. Volz, M. Hassler, H. Schaeffer, *Z. Naturforsch.* **1986**, *41B*, 1265–1272.
29. J. S. Lindsey, H. C. Hsu, I. C. Schreiman, *Tetrahedron Lett.* **1986**, *27*, 4969–4970.
30. J. S. Lindsey, I. C. Schreiman, H. C. Hsu, P. C. Kearney, A. M. Marguerettaz, *J. Org. Chem.* **1987**, *52*, 827–836.
31. C. A. Hunter, L. D. Sarson, *Tetrahedron Lett.* **1996**, *37*, 699–702.
32. T. Arai, K. Kobata, H. Mihara, T. Fujimoto, N. Nishino, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1989–1998.
33. T. Hayashi, T. Asai, F. M. Borgmeier, H. Hokazono, H. Ogoshi, *Chem. Eur. J.* **1998**, *4*, 1266–1274.
34. E. Rose, A. Kossanyi, M. Quelquejeu, M. Soleilhavoup, F. Duwavran, N. Bernard, A. Lecas, *J. Am. Chem. Soc.* **1996**, *118*, 1567–1568.
35. J. Barry, T. Kodadek, *Tetrahedron Lett.* **1994**, *35*, 2465–2468.
36. L. G. Mackay, R. P. Bonar-Law, J. K. M. Sanders, *J. Chem. Soc. Perkin Trans. 1* **1993**, 1377–1378.
37. F. Li, S. I. Yang, Y. Ciringh, J. Seth, C. H. Martin III, D. L. Singh, D. Kim, R. R. Birge, D. F. Bocian, D. Holten, J. S. Lindsey, *J. Am. Chem. Soc.* **1998**, *120*, 10001–10017.
38. K. W. Pollak, E. M. Sanford, J. M. Frechet, *J. Mater. Chem.* **1998**, *8*, 519–527.
39. N. M. Loim, N. V. Abramova, V. I. Sokolov, *Mendeleev Commun.* **1996**, 46–47.
40. H. K. Hombrecher, S. Ohm, D. Koll, *Tetrahedron* **1996**, *52*, 5441–5448.
41. A. Werner, A. Sanchez-Migallon, A. Fruchier, J. Elguero, C. Fernandez-Castano, C. Foces-Foces, *Tetrahedron* **1995**, *51*, 4779–4800.

42. Y. Tokita, K. Yamaguchi, Y. Watanabe, I. Morishima, *Inorg. Chem.* 1993, **32**, 329–333.

43. J. P. Strachan, S. Gentemann, J. Seth, W. A. Kalsbeck, J. S. Lindsey, D. Holten, D. F. Bocian, *Inorg. Chem.* **1998**, *37*, 1191–1201.

44. R. W. Wagner, T. E. Johnson, J. S. Lindsey, *J. Am. Chem. Soc.* **1996**, *118*, 11166–11180.

45. Z. Gross, I. Toledano, *J. Org. Chem.* **1994**, *59*, 8312–8315.

46. E. Rose, M. Soleilhavoup, L. Christ-Tommasino, G. Moreau, *J. Org. Chem.* **1998**, *63*, 2042–2044.

47. T. Imada, H. Kijima, M. Takeuchi, S. Shinkai, *Tetrahedron Lett.* **1995**, *36*, 2093–2096.

48. J. S. Manka, D. S. Lawence, *Tetrahedron Lett.* **1989**, *30*, 6989–6992.

49. M. Ravikanth, J. -P. Strachan, F. Li, J. S. Lindsey, *Tetrahedron* **1998**, *54*, 7721–7734.

50. B. Jiang, S. -W. Yang, D. C. Barbini, W. E. Jones Jr., *Chem. Commun.* **1998**, 213–214.

51. R. L. Halterman, X. Mei, *Tetrahedron Lett.* **1996**, *37*, 6291–6294.

52. T. Akiyama, H. Imahori, A. Ajawakon, Y. Sakata, *Chem. Lett.* **1996**, 907–908.

53. N. Yoshida, H. Shimidzu, A. Osuka, *Chem. Lett.* **1998**, 55–56.

54. M. Taniguchi, A. Balakumar, D. Fan, B. E. McDowell, J. S. Lindsey, *J. Porphyrins Phthalocyanines* **2005**, *9*, 554–574.

55. A. Wiehe, E. J. Simonenko, M. O. Senge, B. Roder, *J. Porphyrins Phthalocyanines* **2001**, *5*, 758–761.

56. X. Feng, I. Bischoff, M. O. Senge, *J. Org. Chem.* **2001**, *66*, 8693–8700.

57. I. Bischoff, X. Feng, M. O. Senge, *Tetrahedron* **2001**, *57* , 5573–5583.

58. M. O. Senge, W. W. Kalisch, I. Bischoff, *Chem. Eur. J.* **2000**, *6*, 2721–2738.

59. C. Ryppa, M. O. Senge, S. S. Hatscher, E. Kleinpeter, P. Wacker, U. Schilde, A. Wiehe, *Chem. Eur. J.* **2005**, *11*, 3427–3442.

60. M. O. Senge, *Acc. Chem. Res.* **2005**, *38*, 733–743.

61. M. O. Senge, X. Feng, *J. Chem. Soc., Perkin Trans. 1* **2000**, 3615–3621.

62. X. Feng, M. O. Senge, *J. Chem. Soc., Perkin Trans. 1* **2001**, 1030–1038.

63. X. Feng, M. O. Senge, *Tetrahedron* **2000**, *56*, 587–590.

64. M. O. Senge, X. Feng, *Tetrahedron Lett.* **1999**, *40*, 4165–4168.

65. M. J. Frampton, H. Akdas, A. R. Cowley, J. E. Rogers, J. E. Slagle, P. A. Fleitz, M. Drobizhev, A. Rebane, H. L. Anderson, *Org. Lett.* **2005**,*7*, 5365–5368.

66. O.B. Locos, D. P. Arnold, *Org. Biomol. Chem.* **2006**, *4*, 902–916.

67. N. Aratani, A. Osuka, *Org. Lett.* **2001**, *3*, 4213–4216.

68. C. -H. Lee, F. Li. K. Iwamoto, J. Dadok, A. A. Bothner-By, J. S. Lindsey, *Tetrahedron* **1995**, *51*, 11645–11672.

69. (a) G. P. Arsenault, E. Bullock, S. F. MacDonald *J. Am. Chem. Soc.* **1960**, *82*, 4384–4389. (b) G. R. Geier, III, J. S. Lindsey, *J. Chem. Soc., Perkin Trans. 2* **2001**, 677–686. (c) G. R. Geier, III, J. S. Lindsey, *J. Chem. Soc., Perkin Trans. 2* **2001**, 687–700. (d) G. R. Geier, III, B. J. Littler, J. S. Lindsey, *J. Chem. Soc., Perkin Trans. 2* **2001**, 701–711.

70. J. B. Paine, III in *The Porphyrins*; D. Dolphin, Ed.; Academic Press. New York, Vol. *1*, pp. 101–234.

71. K. Smith in *The Porphyrin Handbook*; ed by K. M. Kadish, K. M. Smith, and R. Guilard, Academic Press, New York, **2000**, *Vol. 1*, pp. 119–148.

72. C. Ryppa Ph.D. Thesis, *Berlin University (FU)*, **2004**. http://www.diss.fu-berlin.de/2005/49/indexe.html

73. I. Degani, R. Fochi, *J. Chem. Soc., Perkin Trans 1* **1976**, 323–325.

74. D. M. Wallace, K. M. Smith, *Tetrahedron Lett.* **1990**, *31*, 7265–7268.

75. D. M. Wallace, S. H. Leung, M. O. Senge, K. M. Smith, *J. Org. Chem.* **1993**, *58*, 7245–7257.

76. T. Ema, Y. Kuroda, H. Ogoshi, *Tetrahedron Lett.* **1991**, *32*, 4529–4532.

77. T. Mizutani, T. Ema, T. Tomita, Y. Kuroda, H. Ogoshi, *J. Chem. Soc., Chem. Commun.* **1993**, 520–522.

78. P. D. Rao, B. J. Littler, G. R. Geier, III, J. S. Lindsey, *J. Org. Chem.* **2000**, *65*, 1084–1092.

79. P. D. Rao, S. Dhanalekshmi, B. J. Littler, J. S. Lindsey, *J. Org. Chem.* **2000**, *65*, 7323–7344.

80. K. Muthukumaran, M. Ptaszek, B. Noll, W. R. Scheidt, J. S. Lindsey, *J. Org. Chem.* **2004**, *69*, 5354–5364.

81. T. J. Dougherty, *Adv. Photochem.* **1992**, *17*, 275–312.

82. S. B. Brown, T. G. Truscott, *Chem. Br.* **1993**, 955–958.

83. R. A. His, D.I. Rosenthal, E. Glatstein, *Drugs* **1999**, *57*, 725–734.

84. T. J. Dougherty, S. L. Marcus, *Eur. J. Cancer A* **1992**, *28*, 1734–1742.

85. http://www.unine.ch/chim/neier/etudiants/etudiants.html ; Prof. Reinhard Neier, Institut de Chimie, Université de Neuchâtel, Switzerland.

86. R. Bonnett, *Rev. Contemp. Pharmacother.* **1999**, *10*, 1–17.

87. L. Milgrom, S. MacRobert, *Chem. Br.* **1998**, *34*, 45–50.

88. E. S. Nyman, P. H. Hynninen, *J. Photochem. Photobiol. B: Biology* **2004**, *73*, 1–28.

89. http://chemgroups.ucdavis.edu/~smith/PDT_Research/PDT.html

90. C. H. Sibata, V. C. Colussi, N. L. Oleinick, T. J. Kinsella, *Braz. J. Med. Biol. Res.* **2000**, *33*, 869–880.

91. M. R. Detty, S. L. Gibson, and S. J. Wagner, *J. Med. Chem.* **2004**, *47*, 3897–3915.

92. E. J. Dennis, G. C. Dolmans, D. Fukumura, R. K. Jain, *Nat. Rev. Cancer* **2003**, *3*, 380–387.

93. T. J. Dougherty, *Photochem. Photobiol.* **1983**, *38*, 377–379.

94. T. J. Dougherty, W. R. Potter, K. R. Weishaupt, *Prog. Clin. Biol. Res.* **1984**, *170*, 301–314.

95. B. C. Wilson, P. J. Muller, J. C. Yanch, *Phys. Med. Biol.* **1986**, 31, 125–133.

96. G. Jori, *J. Photochem. Photobiol. A* **1992**, *62*, 371–378.

97. M. R. Hamblin, T. Hasan, *Opt. Photonics News* **1996**, *7*, 16–21.

98. R. Bonnett, R. D. White, U.-J. Winfield, M. C. Berenbaum, *Biochem. J.* **1989**, *261*, 277–280.

99. A. M. Richter, B. Kelly, J. K. Chow, D. J. Liu, G. M. N. Towers, D. Dolphin, J. G. Levy, *J. Natl. Cancer Inst.* **1987**, *79*, 1327–1332.

100. J. C. Kennedy, R. H. Pottier, *J. Photochem. Photobiol. B. Biol.* **1992**, *14*, 275–292.

101. R. Bonnett, *Chemical Aspects of Photodynamic Thearpy*; Gordon & Breach: Amsterdam, **2000**.

102. K. Ziegler, H. Zeiser, *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 1847–1851.

103. W. W. Kalisch, M. O. Senge, *Angew. Chem., Int. Ed.*, **1998**, *37*, 1107–1109.

104. T. La, R. Richards, G. M. Miskelly, *Inorg. Chem.* **1994**, *33*, 3159–3163.

105. T. -S. Jin, Y. Zhao, L. -B Liu, Z. Chen, T. -S. Li, *Synth. Commun.* **2006**, *36*, 1221–1227.

106. J. Davila, A. Harriman, L. R. Milgrom, *Chem. Phys. Lett.* **1987**, *136*, 427–430.

107. R. P. Pandian, T.K. Chandrashekar, *Inorg. Chem.* **1994**, *33*, 3317–3324.

108. E. Scamporrino, D. Vitalini, *Macromolecules* **1992**, *25*, 1625–1632.

109. T. Norsten, N. Branda, *Chem. Commun.* **1998**, 1257–1258.

110. R. K. Pandey, N. W. Smith, F. –Y. Shiau, T. J. Dougherty, K. M. Smith, *J. Chem. Soc., Chem. Commun.* **1991**, 1637–1638.

111. A. Osuka, M. Ikeda, H. Shiratori, Y. Nishimura, I. Yamazaki, *J. Chem. Soc., Perkin Trans. 2* **1999**, 1019–1026.

112. J. -P. Tremblay-Morin, H. Ali, J. E. Van Lier, *Tetrahedron Lett.* **2006**, *47*, 3043–3046.

113. K. Sugiura, Y. Fujimoto, Y. Sakata, *Chem. Commun.* **2000**, 1105–1106.

114. J. S. Lindsey, S, Prathapan, T. E. Johnson, R. W. Wagner, *Tetrahedron* **1994**, *50*, 8941–8968.

115. R. W. Wagner, T. E. Johnson, F. Li, J. S. Lindsey, *J. Org. Chem.* **1995**, *60*, 5266–5273.

116. (a) B. Krattinger, H. G. Callot, *Tetrahedron Lett.* **1996**, *37*, 7699–7702. (b) B. Krattinger, H. G. Callot, *Tetrahedron Lett.* **1998**, *39*, 1165–1168.

117. S. P. Foxon, J. R. L. Smith, P. O`Brien, G. Reginato, *J. Chem. Soc. Perkin Trans. 2* **2001**, 1145–1153.

118. R. J. Abraham, *Mol. Phys.* **1961**, *4*, 145–152.

119. P. J. Chmielewski, L. Latos-Grazynski, K. Rachlewicz, *Magn. Reson. Chem.* **1993**, *31*, S47-S52.

120. B. Boitrel, A. Lecas and E. Rose, *J. Chem. Soc., Chem. Commun.* **1989**, 349–350.

121. S. Klod, E. Kleinpeter, *J. Chem. Soc., Perkin Trans. 2* **2001**, 1893–1898.

122. R. Ao, L. Kummerl, D. Haarer, *Adv. Mater.* **1995**, *7*, 495–499.

123. H. S. Nalwa, *Adv. Mater.* **1993**, *5*, 341–358.

124. R. J. Mortimer, *Chem. Soc.Rev.* **1997**, *26*, 147–156.

125. S. Runge, M. O. Senge, *Tetrahedron* **1999**, *55*, 10375–10390.

126. M. O. Senge, I. Bischoff, *Eur. J. Org. Chem.* **2001**, 1735–1751.

127. J. Meisenheimer, *Ber.* **1935**, *68*, A32–A33.

128. A. Treibs, N. Häberle, *Liebigs Ann. Chem.* **1968**, *718*, 183–207.

129. C. Brückner, J. J. Posakony, C. K. Johnson, R. W. Boyle, B. R. James, D. Dolphin, *J. Porphyrins Phthalocyanines* **1998**, *2*, 455–465.

130. R. C. Verboom, V. F. Slagt, J. E. Baeckvall, *Chem. Commun.* **2005**, *10*, 1282–1284.

131. J. S. Lindsey in *The Porphyrin Handbook*; ed by K. M. Kadish, R. Guilard, and K. M. Smith, Academic Press, San Diego, **2000**, *Vol. 1*, pp. 45–118.

132. A. D. Joran, B. A. Leland, G. G. Geller, J. J. Hopfield, P. B. Dervan, *J. Am. Chem. Soc.* **1984**, *106*, 6090–6092.

133. A. Osuka, R. P. Zhang, K. Maruyama, I. Yamazaki, Y. Nishimura, *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2807–2813.

134. J. Arnold, D. Y. Dawson, C. G. Hoffman, *J. Am. Chem. Soc.* 1993, *115*, 2707–2713.

135. M. O. Senge, S. Runge, M. Speck, K. Ruhlandt-Senge, *Tetrahedron*, **2000**, *56*, 8927–8932.

136. J. L. Hoard, *Ann. N. Y. Acad. Sci.* **1973**, *206*, 18–31.

137. A. J. Golder, L. R. Milgrom, K. B. Nolan, D. C. Povey, *J. Chem. Soc., Chem. Commun.* **1989**, 1751–1753.

138. D. G. Farnum, Jr. C. F. Wilcox, *J. Am. Chem. Soc.* 1967, *89*, 5379–5383.

139. A. T. Balaban, A. Dinculescu, I. F. Antonie, F. Chiraleu, D. Patrascoiu, *Chem. Scripta* **1981**, *18* , 230–232.

140. R. J. Abraham, J. Plant, *Org. Magn. Reson.* **1982**, *19*, 204–210.

141. P. D. Rao, S. Dhanalekshmi, B. J. Littler, J. S. Lindsey, *J. Org. Chem.* **2000**, *65*, 7323–7323.

142. J. S. Lindsey in *Metalloporphyrins Catalyzed oxidations*; F. Montanari, L.casella Eds.; Kluwer Academic: Dordrecht, **1994**; pp. 49–86.

143. L. Sun, J. van Gersdorff, D. Niethammer, P. Tian, H. Kurreck, *Angew. Chem.* **1994**, *106*, 2396–2399; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2318–2320.

144. C. -H. Lee, J. S. Lindsey, *Tetrahedron* **1994**, *50*, 11427–11440.

145. C. Brückner, D. Dolphin, *Tetrahedron Lett.* **1995**, *36*, 3298–3298.

146. F. Rancan, A. Wiehe, M. Nöbel, M. O. Senge, S. Al Omari, F. Böhm, M. John, B. Röder, *J. Photochem. Photobiol. B* **2005**, *78*, 17–28.

147. Y. Chen, C. J. Medforth, K. M. Smith, J. Alderfer, T. J. Dougherty, R. K. Pandey, *J. Org. Chem.* **2001**, *66*, 3930–3939.

148. B. Krattinger, H. G. Callot, *Eur. J. Org. Chem.* **1999**, 1857–1867.

149. F. Li, K. Yang, J. S. Tyhonas, K. A. MacCrum, J. S. Lindsey, *Tetrahedron* **1997**, *53*, 12339–12360.

150. J. L. Sessler, A. Mozaffari, M. R. Johnson, *Org. Synth.* **1992**, *70*, 68–78.

151. S. Neya, N. Funasaki, *Tetrahedron Lett.* **2002**, *43*, 1057–1058.