Total synthesis of cofacial chlorin dimers of two different symmetries

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Models of photosynthetic reaction centers

Thesis

Submitted as partial fulfilment of the requirement
for the degree
Doctor of Natural Sciences
(Doktor der Naturwissenschaften)
(Dr. rer. nat.)

Faculty of Biology/Chemistry, University of Bremen

April 2011

By

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Bremen 2011

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Date of doctoral examination: May 10th, 2011

ACKNOWLEDGEMENT

First of all, I would like to express my sincere gratitude to my supervisor Prof. Dr. Franz-Peter Montforts for his excellent advising from my very first to my final steps in conducting the work leading to this thesis. Under her supervision I became stronger in developping ideas as well as joining the research community.

I owe immense thanks to persons for their technical support: Mr. Johannes Stelten (Dipl.-Ing) for NMR tutorial lessons and NMR analysis; Dr. Thomas Dülcks and Mrs. Dorit Kemken (Dipl.-Ing.) for the mass spectra measurements; Dr. Tobias for the theoretical calculations and explanation.

I sincerely thank all colleagues in AK Montforts who create a wonderful environment for research and living, especially in many interesting social events: Dr. Martina Osmer, Dr. Stephan Leupold, Dr. Vladimir Azov, Dr. Doan Duy Tien, Dr. Thorsten Könekamp, Dr. Jan-Erick Damke, Dr. Babara Maria Panek-Bryla, Dr. Christoph Eberle and Dipl.-Chem. Dennis Leupold (my wonderful labmates), Dipl.-Chem. Daniela Bauer, Dipl.-Chem. Yvonne Neumann, Dipl.-Chem. Martin Erbacher, Dipl.-Chem. Torben König, Dipl.-Chem. Matthias Düker, M.Sc Nghiem Hai Vu, M.Sc. Rudy Martin, M.Sc. Joana Cabrita, Dipl.-Chem. Emrah Görüs, Dipl.-Chem. Kathrin Lummer, Dipl.-Chem. Kerstin Geller, Mrs. Ursula Lücking. I am also very grateful to Mrs. Ursula Montforts.

I extend thanks to MOET, DAAD as the two crucial financial sources for my thesis work. I also thank DAAD for the practical support during my studies in Germany such as annual meetings and policies in administration procedures.

Last but not least, I am very lucky to have had many close friends to support me to get through the rough time. The study time in Bremen has made me realize more than ever how much my family means to me. I dedicate this dissertation to them.

Bremen, 30. January 2011

Nguyen Thi Viet Thanh

TABLE OF CONTENTS

1. INTRODUCTION

1.1 PHOTOSYNTHESIS

Photosynthesis is the process which converts light energy into chemical energy together with the transformation of CO_2 to organic compounds, commonly carbohydrates. Photosynthetic systems are present in plants, algae and many species of bacteria. The bacterial photosynthetic center is based on one photosystem which does not produce oxygen while the plant photosynthetic center makes use of two photosystems named photosystem I (PSI), photosystem II (PSII) and generates oxygen.[1] In photosynthesis, light is absorbed by light-harvesting complexes then excitation energy transferred efficiently and rapidly to the photosynthetic reaction center (RC), where a charge separation and electron transfer to reactive species occur.

1.1.1 Bacterial Photosynthesis

Although photosynthesis is present mainly in plants and algae, the best understanding of the photosynthetic mechanism was based on the knowledge of bacterial RCs. The X-ray structures of photosynthetic reaction centers from *Rps. viridis* and *Rb. sphaeroides* were first determined by Johann Deisenhofer, Robert Huber and Hartmut Michel (the Nobel Prize in chemistry, 1988).[2] The investigation offered the structural and functional characterizations of the bacterial photosynthetic system at the molecular level.

The RC of *Rps.viridis* (Fig. 1) comprises four protein subunits named L (light) (maroon), M (medium) (yellow), H (heavy) (purple), and cytochrome, and 10 cofactors. The L and M protein bind the cofactors in the core and arrange them in two branches L and M, but only one branch is active in the electron transfer process.[2-4] The origin of the two branches is a pair of bateriohlorophylls *b* (BChls-*b*) termed D_L and D_M. They are called special pair (SP), which is associated with two accessory bacteriochlorophyll *b* (B_A, B_B), bacteriopheophytins (Φ_A, Φ_B) (BChl without central Mg), one menaquinone-9 (Q_A), one ubiquinon-9 (Q_B), a carotenoid and a non-heme iron complex (referring to center Fe and its ligands without any heme). The size of the RC was determined clearly with a distance from the top of cytochrome to the bottom of protein H subunit of about 130 Å. The cofactor complex form is elliptical with the length of the two axes of about 70 Å and 30 Å.

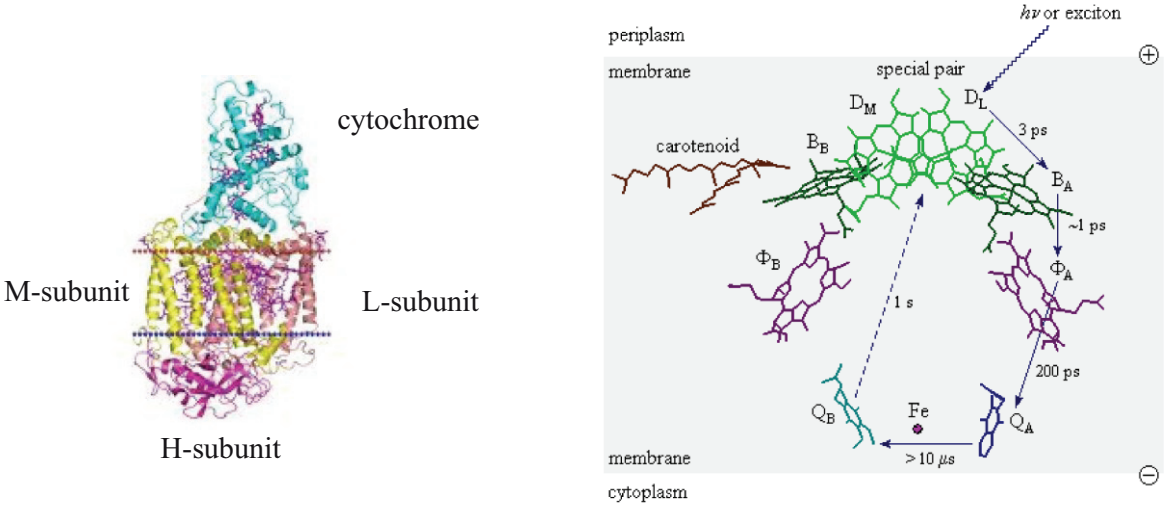


Figure 1: The photosynthetic reaction center of *Rps. Viridis*[3]

a): The reaction center with the four protein subunits: M (medium), H (heavy), L (light) and Cyt (cytochrome c).

b): The cofactors of the reaction center: pair of bacteriochlorophylls (D_M, D_L), accessory bacteriochlorophylls (B_B, B_A), Bacteriopheophytins (Φ_A, Φ_B), menaquinone (Q_A) and ubiquinone (Q_B).

From the electron transfer process of bacterial RC described in Fig. 2, light is absorbed by light harvesting antennas surrounding the reaction center. The energy is then transferred to the special pair SP, functioning as the donor, to raise it to the excited state SP*. This process is followed by the transfer of one electron to the Φ_A via the accessory B_A along the L-branch with a rate of 2.8 ps. From Φ_A, the electron moves rapidly to the Q_A with the time constant of 200 ps. This quinone slowly passes the electron to the secondary quinone (Q_B) through nonheme ion complex (100μs). The Q_B can take 2 protons from the cytoplasm to form dihydroquinone (Q_BH_2). The electron transfer process can also be described following:

$$SP \rightarrow SP^*$$

$$SP^* + B_A \rightarrow SP^{\cdot +} + B_A^{-}$$

$$B_A^{\cdot -} + \Phi A \rightarrow B_A + \Phi_A^{\cdot -}$$

$$\Phi A^{\cdot -} + Q_A \rightarrow \Phi A + Q_A^{\cdot -}$$

$$Q_A^{\cdot -} + Q_B + 2H^+ \rightarrow Q_A + Q_BH_2$$

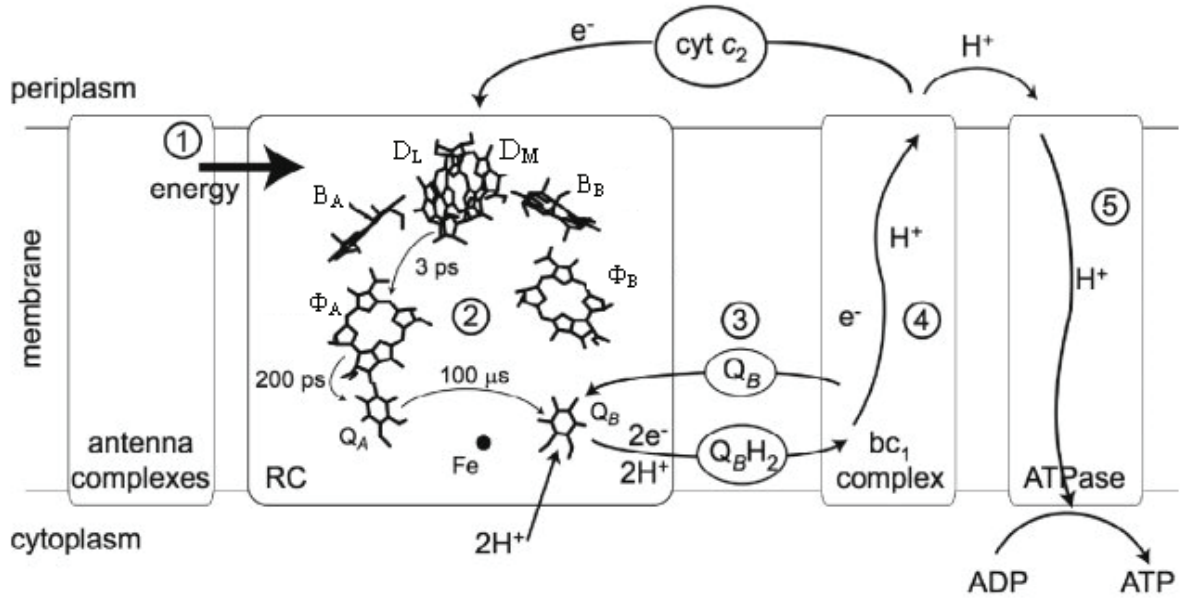


Figure 2: The photosynthetic process of a typical purple bacterium [5]

D_L, D_M, B_A, B_B: Bacteriochlorophyll, Φ_A, Φ_B: Bacteriopheophytine, Q_A, Q_B: quinone, Q_BH_2: dihydroquinone, cyt c_2: cytochrome c_2.

(1): energy transfer from antenna to RC, (2): the charge separation and transportation among RC subunits, (3): the release of Q_BH_2 and refill of Q_B between RC and quinone pool in membrane, (4): oxidation of Q_BH_2 resulting the electron transport along cyt c_2 to SP and proton across the membrane, (5) the proton driving process for ATP synthesis.

The Q_BH_2 is isolated from the RC and the Q_B is refilled from the quinone pool in the membrane. The electrons on the Q_BH_2 are transferred back through the cytochrome c_2 to the cytochrome with the time constant of ~270 µs, to re-reduce SP^+ to SP. The proton on Q_BH_2 transfers across the membrane to parcitipate in the ATP synthesis process.

However, some questions of the electron transfer mechanism remain are still unexplained, such as the roles of the B_A, B_B, the non-heme iron complex, and details of electron transport process from soluble cytochromes.

1.1.2 Plant photosynthesis

Photosynthesises of plants and green algae produce oxygen and organic materials from CO_2 and water. This procedure provides food and fuel, and has determined the climate of the Earth for billions of years.

The photosynthesis apparatus of plants contains two reaction center complexes termed photosystem I (PSI), which drives the transformation CO_2 to carbohydrate, and photosystem

II (PSII) which splits water to form oxygen. The whole process of plant photosynthesis is described in Fig. 3.

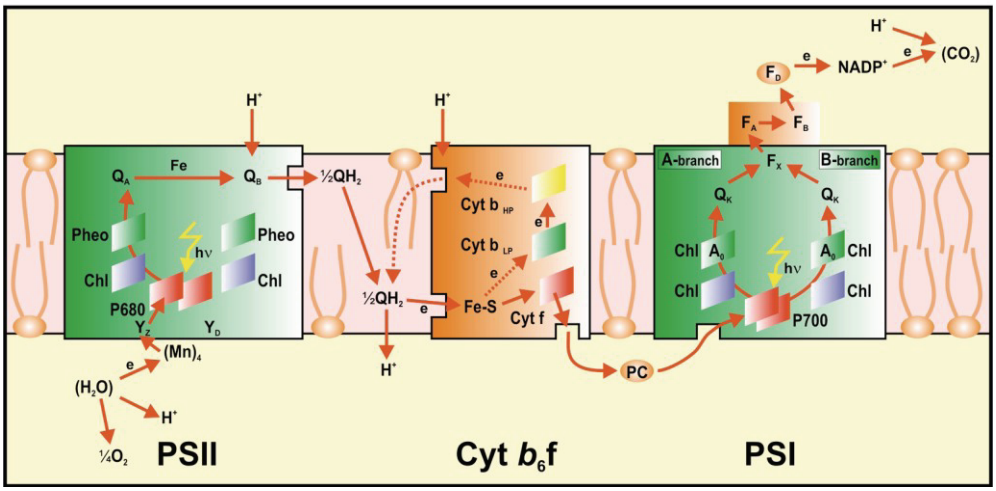


Figure 3: The photosynthetic apparatus of plants[6]

PSII: Photosystem II, Cyt b_6f: Cytochrome b_6f, PSI: Photosystem I

The electron transport chain of plant photosynthesis is shown in Fig. 4. This diagram reveals how photosystem I (PSI) and photosystem II (PSII) work together absorbing light for oxidation of water and reduction of $NADP^+$.

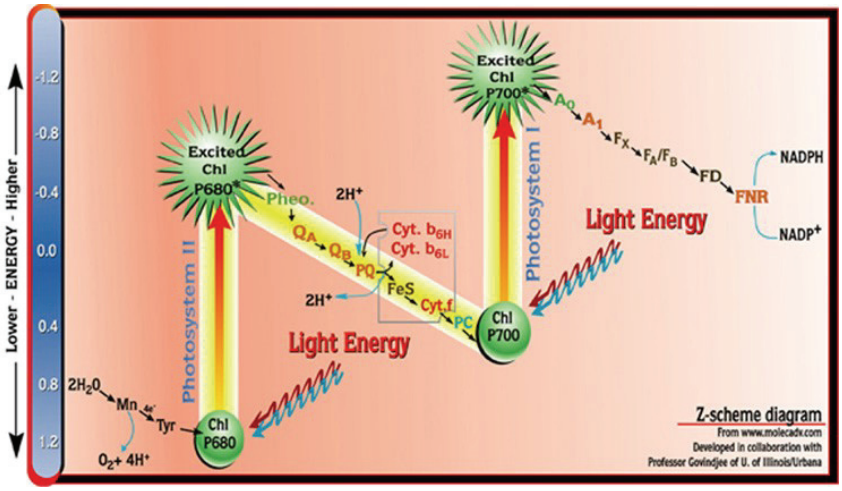


Figure 4: The light-induced electron pathway in the SPII and SPI of a higher plant [7]

Details of the whole photosynthetic process could be obtained by the analysis of the structures and the electron transport mechanism in PSI and PSII following.

Photosystem II (PSII)

Photosystem II is a multi-protein complex composed of more than 20 protein subunits, at least 44 cofactors including chlorophylls and carotenoids, two pheophytins, plastoquinones, lipids, components of the Mangan cluster, and one Fe^{2+} (Fig. 5). The arrangement and the electron transfer in the core of PSII are quite similar to bacterial photosynthesis. Two chlorophyll *a* molecules termed P_{D1} and P_{D2}, two chlorophylls Chl_{D1}, Chl_{D2} and plastoquinone are equivalent to the 'special pair', accessory bacteriochlorophylls, and quinones, respectively, of the bacterial RC. However, the P_{D1} and P_{D2} are further apart than the two found in their bacterial counterparts.[8-9]

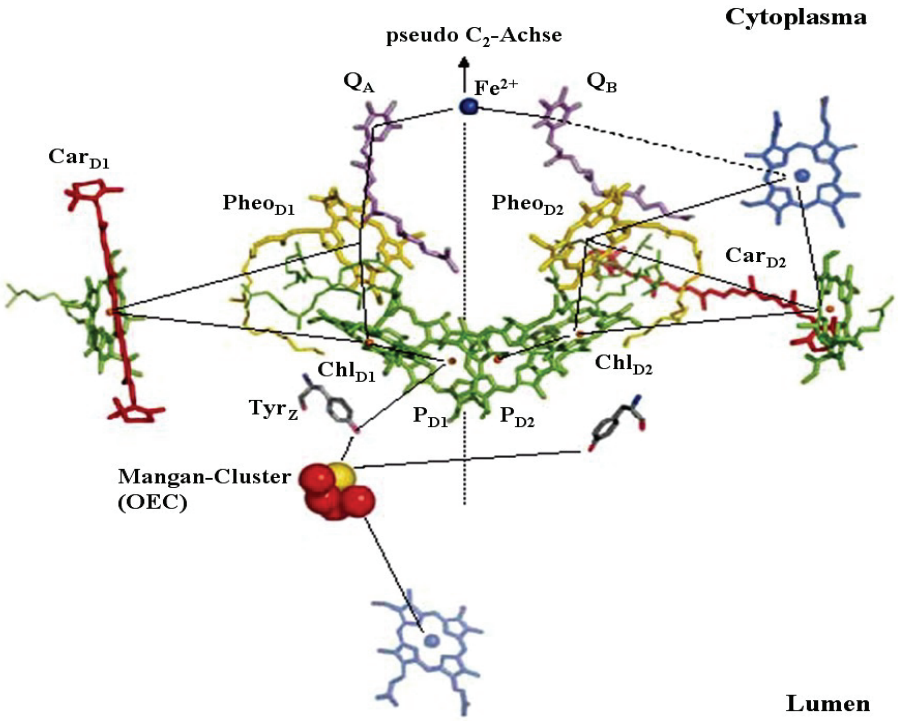


Figure 5: The spatial arrangement of the cofactors regarding the electron transfer chain in PS II[9]
$P_{D1}/P_{D2}/Chl_{D1}/Chl_{D2}$: chlorophylls; $Pheo_{D1}/Pheo_{D2}$: pheophytin, QA / QB: plastoquinones; TyrZ: tyrosine; CarD1/CarD2: carotenoids

After being absorbed by antenna, light energy is transferred to the reaction center resulting in the excitation of primary electron donor P680 to excited state P680*. It is not clear if P680 comprises $P_{D1}$and P_{D2} or P_{D1}, P_{D2}, Chl_{D1} and Chl_{D2}. One electron from P680* is released and travels along the electron chain by means of chlorophyll *a* (Chl_{D1} or Chl_{D2}), pheophytin *a* (PheoD1), plastoquinone Q_A, forming $P680^{+\cdot}Q_{A-\cdot}$. The electron partcitipates in two further steps of reduction and protonation of the secondary plastoquinone QB. The plastoquinol Q_BH_2

is formed then released to the platoquinone pool in the membrane. These processes are similar to the electron transfer in bacterial RC. Q_BH_2 is then oxidized at the cytochrome b6f to plastoquinone Q_B. The electron gained after this oxidation is transferred to the plastocyanine to form the electron chain in PSI. At the oxidised side of SPII, the $P680^+$ takes one electron from a Mn cluster by means of a redox-active tyrosine residue (D1-Tyr-161) (Tyrz) to be reduced to P680 for another photosynthetic cycle. In turn, the Mn cluster withdraws an electron from a water molecule leading to the oxidation of water to form oxygen and a proton (see Fig. 3, 4). This reaction provides oxygen generation for the atmosphere.[10-13]

Photosystem I (PSI)[14-26]

Photosystem I contains 11-14 proteins and different types of cofactors including organic and inorganic compounds. Chlorophyll is the most abundant component of PSI.

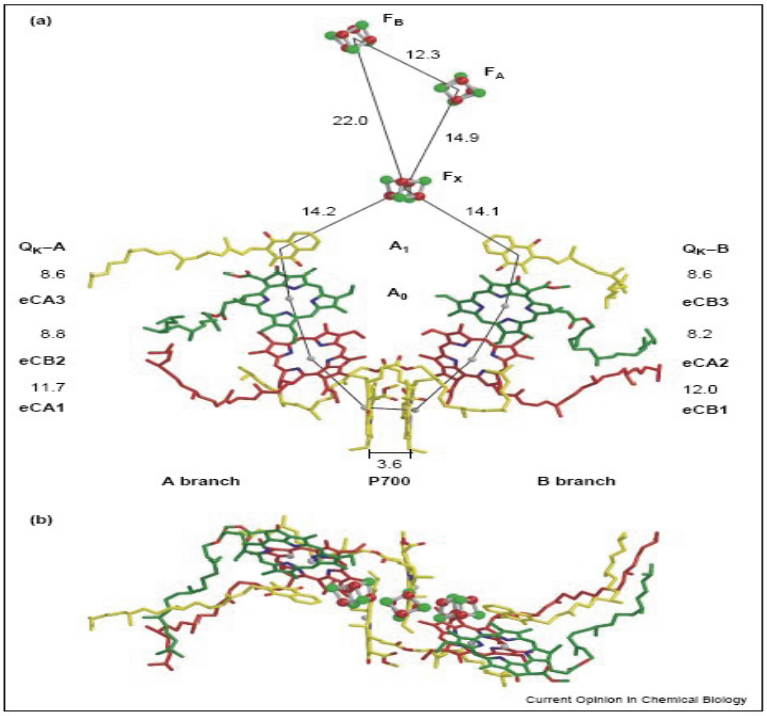


Figure 6: The structure of the PSI core with two branches A, B of electron transfer[15]

P700: SP, two assessory chlorophylls (red color), A_0: chlorophylls *a* as the primary acceptor. A_1: phylloquinone, clusters FX, F_A and F_B

It is until today not clear which oneof the two branches or if both of them are involved in the electron transfer process. There are two sets of accessory chlorophylls *a*, termed A. The second chlorophylls *a* as the first acceptor is termed A_0 and phylloquinone functional as the redox center A_1. The two branches are symmetrically arranged along a central axis. PSI

contains also 3 iron-sulphur complex (Fe–S) clusters, termed FX, F_A and F_B. They function as intermediate cofactors to transport electrons to ferredoxin (F_D), that parcitipates in the CO_2 transformation.

The PSI undergoes the electron transfer from plastocyanine (PC) to ferredoxin, resulting in the reduction of $NADP^+$. After the light is absorbed by antenna, the energy is transferred to the special pair P700, which traps energy and subsequently donates an electron to the acceptor. The primary charge separation occurrs probably from the electronically excited P700 (P700*) to primary acceptor A_0 through the intermediate accessory chlorophyll *a* (A) (Fig. 6). This process is followed by electron transfer to phylloquinone A_1 then to clusters FX, FA and FB. It is accepted that the electron is transferred from Fx through F_A, F_B to ferredoxin. The reduced ferredoxin is an essential redox center used in many chloroplast reactions, especially the reduction of $NADP^+$ to NADPH. NADPH and ATP then provide the chemical energy for the transformation of CO_2 to organic compounds. In turn, the oxidant $P700^+$ abstracts one electron from plastocyanine forming P700 to drive the next electron transport chain.

1.2 (BACTERIO)CHLOROPHYLL SPECIAL PAIR OF THE PHOTOSYNTHETIC REACTION CENTER

The (bacterio)chloropyll dimer occurs at the heart of RC termed special pair (SP). It functions as the donor, the starting point of the light driven electron transfer chain in RC. In purple bacteria, SP absorbs photons at 870 nm, thus, it is called P870 with P standing for "pigment". Similarly, SP is termed P700 in photosystem I (PSI).[27] In the photosystem II (PSII) of cyanobacteria, algae, or plants, it is under debate that SP is the primary donor termed P680 or there is no SP. The one electron oxidation potential of P680 is 1.1-1.2 V, very different in comparison with 0.49 V of P700 and 0.45 of P870.[28] According to Marcus theory (Nobel price in chemistry 1992),[29-31] the electron transfer rate depends on three factors: the overlap of electron densities of molecules, the redox potential between donor and acceptor, and the reorganization energy relating to the energy of rearrangement of atoms within molecules. The theory states that the slightly overlapped electronic orbitals are efficient for the reaction involving the electron transfer between reacting molecules.

The properties of P870

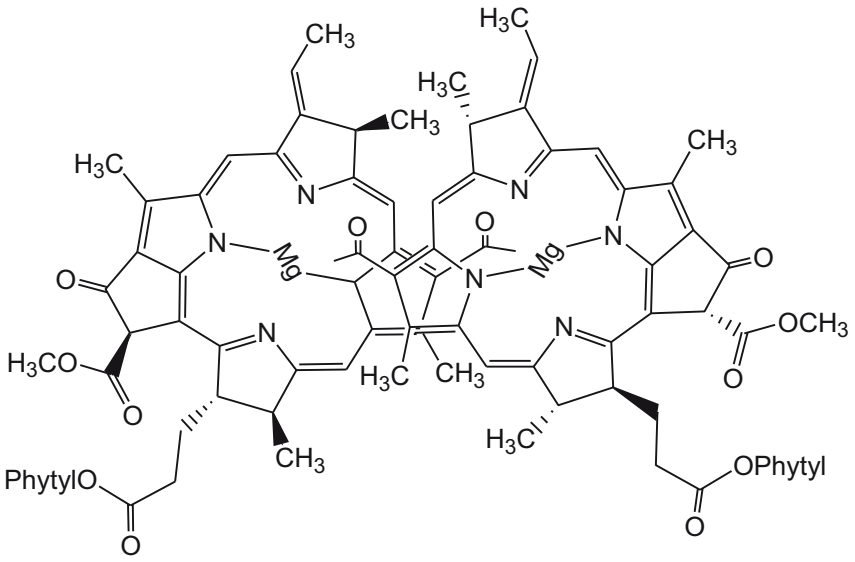


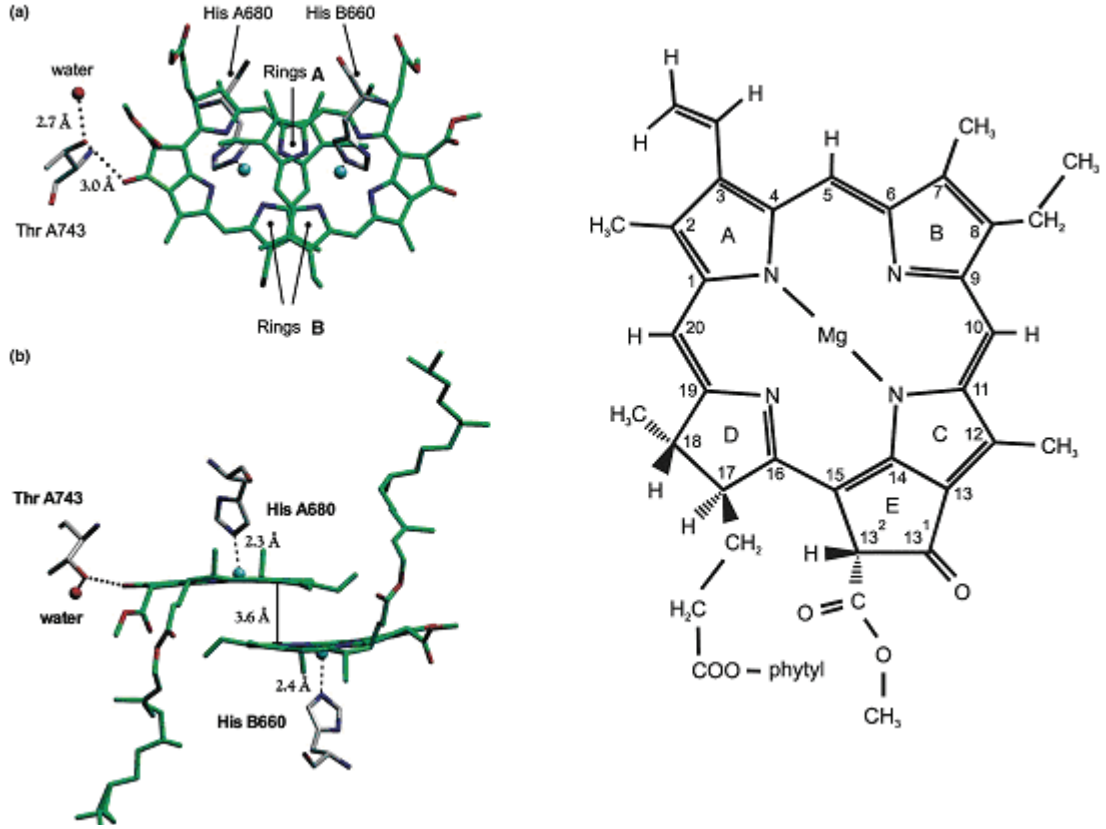
Figure 7: The structure of special pair in bacterial reaction center

The two molecules overlap at their pyrrole rings A (Fig. 7) in such a way that, when looking in a direction perpendicular to the ring planes, the atoms of these rings eclipse each other.

The pyrrole rings A of both BChls-*b* are nearly parallel, and about 3.2 Å apart. The distance from center to center of the two macrocycles is 7.6 Å. Both tetrapyrrole macrocycles, however, are non-planar, the planes through the pyrrole nitrogens of each BChl-*b* form an angle of 11.3º. The BChl (D_M) ring is considerably more deformed than that of BChl (D_L) (see Fig. 1). This can cause an unequal charge distribution between the two components of the special pair, which in turn can be one of the reasons for unidirectional electron transfer.[2,32] The SP of bacteria RC inherits space, thus the electron density overlaps and the difference of redox potential between donor SP and acceptor Φ_A is essentially influenced for transfering electrons.[33] Moreover it is bounded rigidly by proteins, keeping the donor reorganization energy small.

1.2.1 The properties P700

The primary electron donor of photosystem I structure termed P700 is obtained from the X-ray crystallographic structure analysis at 2.5 Å resolution.[34]



1 **2**

Figure 8: The spatial structure of P700 bounded by local amino acids at 2.5 Å resolution [34]

1) Top (a) and side (b) view of chlorophyll dimer

2) Molecular structure and IUPAC numbering scheme for chlorophyll a (Chl a). Chl a' is the 13^2 epimer of Chl

Fig. 8 indicates that P700 is a dimer composed of one Chl *a* and one Chl *a'*, 13^2 epimer of Chl *a* (Fig. 8). These two chlorophyll macrocycles overlap at two corresponding rings A and ring B. The average distance between two planes is about 3.6 Å. P700 is surrounded by proteins but hydrogen bond is found only between proteins and Chl *a*'. The absorption spectrum of P700 shows a red shift compared to Qy transition of chlorophyll in solution. That could be an additional evidence of P700 as a dimer with the interaction between two chlorophylls. The orientations of the Chlorophyll *a* in P700 and the Bchl in purple bacteria are very similar. This reveals the same origin of the photosynthetic systems. However, the electronic and chemical structure of P700 is not yet clear. Some questions are still not answered, such as the role of the H-bondings, whether an electron is transfered from P700 into both branches in RC or only into one side.[34-39]

1.2.2 The properties of P680

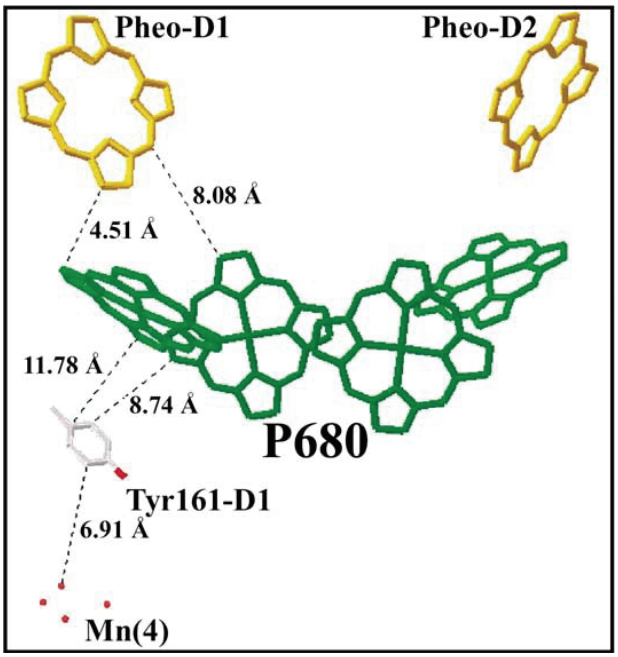


Figure 9: Organization of the donor in PSII from *Synechococcus elongates* at 3.8 Å resolution [40]

The primary electron donor of photosystem II termed P680 is composed of chlorophylls *a*. The structure of P680 is still under debate. J. Barber *et al.*[40,41] suggested that four attributers including P_{D1}, P_{D2} and two accessory chlorophylls *a* were approximately equidistant from each other, with a centre-to-centre distance of about 10–11 Å, further in comparison of the

corresponding bacteriochlorophylls in bacterial SP. The two chlorophylls, equivalent to the 'special pair', were spaced further apart than those found in their bacterial counterparts (10 to 11 Å in PSII compared with 7 Å in bacteria, based on centre-to-centre distance). The authors also stated that all other types of SP show the redox potential of 0.5 V or less. However, P680 radical had an outstanding redox potential of 1 V or more. This requires that all four chlorophylls in the PSII reaction center have high redox potentials when oxidised. Therefore, a monomeric form of chlorophyll is necessary in order to develop a redox potential for the oxidation of water.

In contrast, a study of crystal structure of Photosystem II from *Thermosynechococcus vulcanus* at 3.7 Å resolution by Nobuo Kamiya and Jian-Ren Shen [42] indicated that the closest distance between P_{D1} and P_{D2} was 4 Å, shorter than the closest distance from these chlorophylls to the Chl_{D1} of 5 Å (Fig. 10). The overlapped space between P_{D1} and P_{D2} is larger than the corresponding space between P_{D1}, Chl_{D1} and P_{D2}, Chl_{D2} as well. This suggests that P_{D1} and P_{D2} interact with each other stronger than with Chl_{D1} and Chl_{D2}.

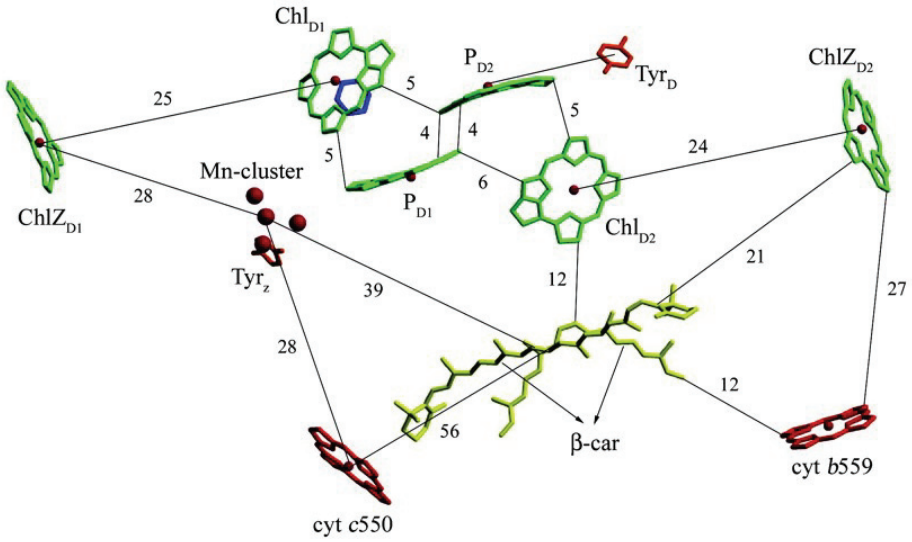


Figure 10: Arrangement of the special pair and other cofactors from *Thermosynechococcus vulcanus* at 3.7 Å resolution [42]

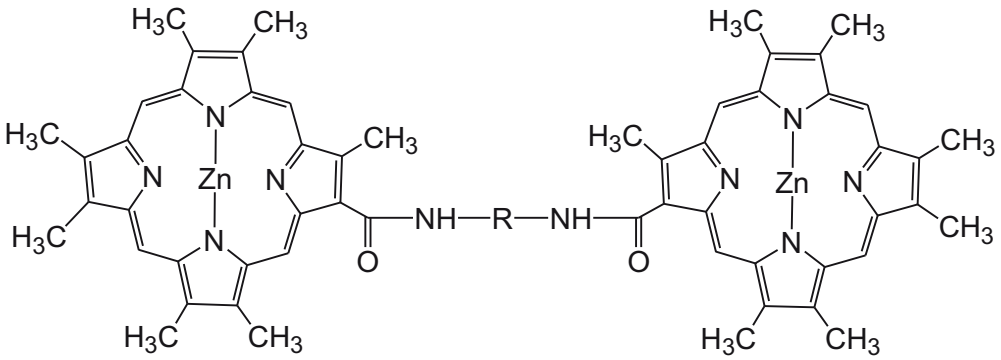
1.3 MOLECULAR SYSTEMS FOR MODELLING NATURALLY OCCURRING SPECIAL PAIRS

The investigations of the structure and the electronic mechanism of the reaction center and the SP are still in progress. Thus mimicking the reaction center and in particular the SP have attracted scientists in the field of artificial photosynthesis in recent decades. The main aim of these researches is the better understanding of the photo initiated-electron-transfer reactions by simplifying the SP in laboratory models.[43]

A well designed model depends on the selection of chromophores and the linkage between them. The chromophors should be selected from natural pigment such as chlorin, chlorophyll, bacterial chlorophyll. The efficient linkage is determined by the spatial and the angular relation to mimic protein bouding chlorophyll.[44]

Although numerous models accounting for artificial photosynthetic system were reported, the major models were based on covalently linked porphyrins to mimic antenna complexes or donor-acceptor systems of RCs. Porphyrin-based models mimicking SP of RC regarding their similarity compared to natural structures are limited.[45]

The first artificial model of SP based on tetrapyrroles was published by Schwartz *et al.* [46,47] in 1972 (Fig. 11). This artificial SP was based on two porphyrins which were connected each other via an amide group.



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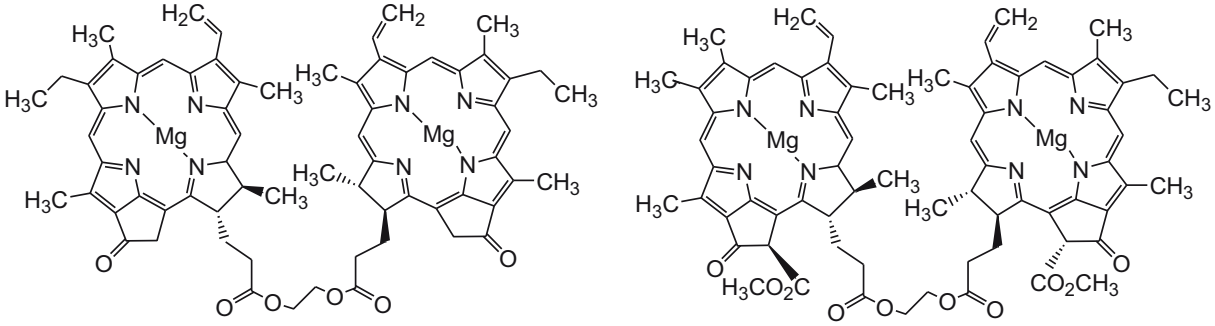
R is ethylene or *p*-phenylene

Figure 11: Model **1** of SP based on the metallporphyrins

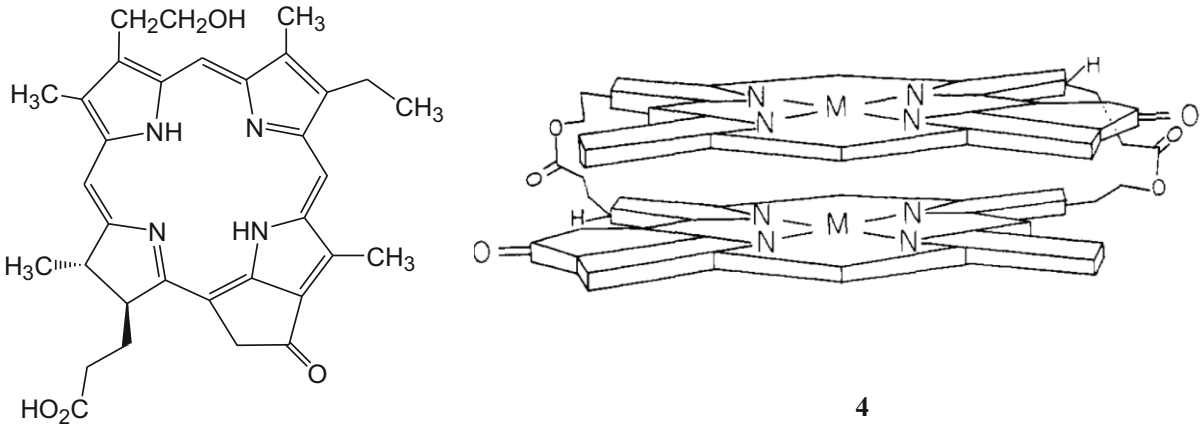
Wasielewski *et al.* prepared a bis-pyrochlorophyllide **2** successfully.[48] In the synthetic process, pyropheophorbide free acid was esterified with ethylene glycol to form pyropheophorbide *a* ethylene glycol monoester, which was then linked with another pyropheophorbide free acid again by the second ester bond. The same synthetic pathway was employed to yield bis-chlorophyllide **3**. However, both dimers showed similar or decreasing fluorescent lifetimes and quantum yield compared to monomeric subunits.



2 **3**

Figure 12: The structure of the covalently bound dimers of pyrochlorophyllide *a* **2** (a), chlorophyllide **3** (b)

Another model chlorophyll SP is bis(chlorophyll)cyclophane **4,**[49] in which two chlorophyll derivatives were bound by 2 covalent linkages (Fig. 13). This dimer underwent the one-electron oxidation more easily than the chlorophyll monomer.



4

Figure 13: The Bis(chlorophyll)cyclophanes (**4**) as model of SP in photosynthetic reaction center [49]

Osuka *et al.* developed models of SP based on porphyrins. They linked each other via a disubstituted phenyl bridge (Fig. 14).[50]

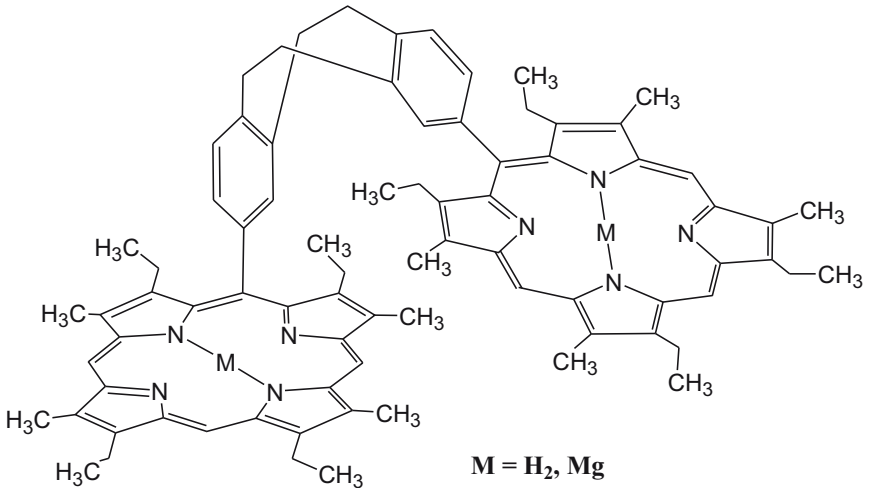
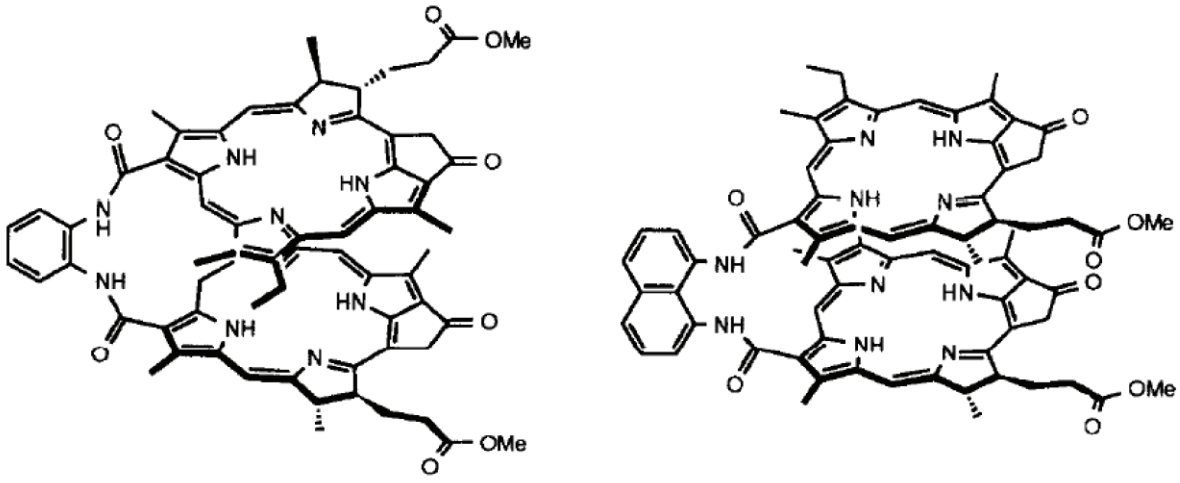


Figure 14: Arrangement of a porphyrin dimer **5** with a fixed distance

In the model, two porphyrins are partially overlapped with each other at one pyrrole ring with a vertical separation of ca. 4 Å, the dihedral angle between two planes is about 10-35^{o} and the center to center distance of two monomers is ca. 10 Å. This conformation is relatively similar to the SP of *Rhodoseudomonas viridis* bacterial RC.

One electron oxidation potential of Mg-porphyrin dimer and Mg-porphyrin were measured in butyronitrile as 0.12 V and 0.16 V, respectively. The author implied that the oxidation potential of this SP model may be achieved by the delocalization of an unpaired electron over both porphyrin monomers. This result demonstrated the similar charater of the model as the SP in vivo.

Another attempt to mimic SP was also achieved by Osuka *et al.*.[51]



6 **7**

Fig 15: The pheophorbide dimers linked by the benzene derivatives, **6**: benzene, **7**: naphthalene as the bridges[51]

This model is based on 3-devinyl-3-carboxylpyropheophorbide-*a* as the monomer subunit. A benzene or naphthalene spacer was employed as the bridge in order to link two chromophores in the cofacial dimer using an ester linkage. The redox potential of both dimeric models shifted to lower value compared to corresponding monomer (0.06 V of **6** and 0.15 V of **7**). These shifts were larger compared to the model reported by Wasielewski *et al.* (0.06 V). The author implied that this shift depended on the geometry of the dimer, and this result was similar to the difference between redox potential of bacterochlorophyll *a* and SP in *Rhodoseudomonas viridis* bacterial photosynthesis reaction center.

Ganzeng *et al.* has developed porphyrin-based models[45] with the geometry, orientation and π electron system sufficiently similar to the SP in bacteria (Fig. 16). In this study, two monomer subunits were employed as chlorins or bacteriochlorins and they were linked by a spacer unit. Dimer **8** was unstable and converted to dimer **9**. The NMR upfield shift of N-H proton of unexpected dimer **9** revealed a remarkable electron π overlap. The X-ray structure determination indicated that the spatial separation between chlorin subunits of **9** (3.4 Å) was in the same range as found in SP (3.1-3.6 Å). The dihedral angle between two chlorins in **9** was about 3°. This determined the dimer more planar than bacterial SP (about 11°). The author also stated that if focusing only on the relative orientation and space overlap between rings, the behaviour of the dimer **9** is very similar to SP in bacterial reaction center.

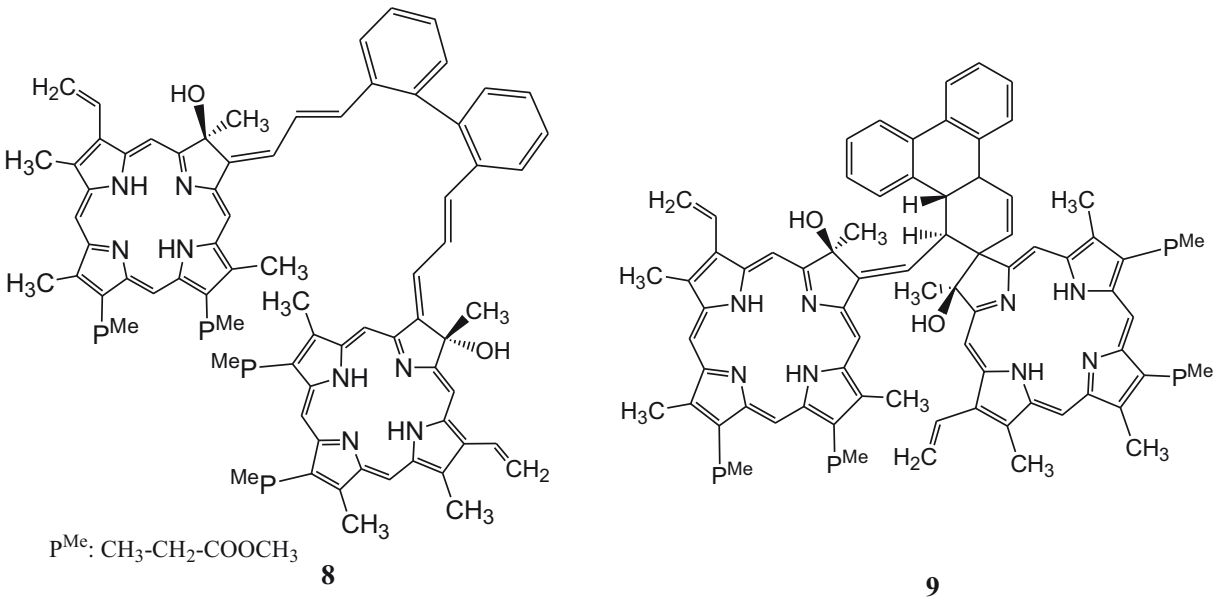


Fig 16: Artificial bacterial chlorophyll dimers as models for reaction centers: bis-chlorin model system **8**, unexpected chlorin-spurichlorin dimer **9**

2. RESEARCH OBJECTIVES

2.1 DESIGN OF COFACIAL CHLORIN DIMERS MIMICKING SPECIAL PAIRS

This project focuses on well-defined models of SP which are spatially and electronically similar to the natural bacteriochlorophyll and chlorophyll dimers occuring in bacteria and plant reaction centers. When invoking models that mimic the reaction center and the SP, numerous systems based on porphyrin were designed. However these models indicated that they have only limited validity compared to models based on natural chlorin pigments, which exhibit low symmetry with respect to a low S_1 energy state, strong Q absorption band, leading to a higher potential for electron and energy transfer. Therefore various chlorin dimers of different symestries were designed to mimic the special pair (Fig. 17).

In the *cis*- arrangement, the saturated pyrrole rings of chlorin are adjacent orientation and in the *trans*-arrangement the saturated pyrrole rings of chlorin are opposite orientation.

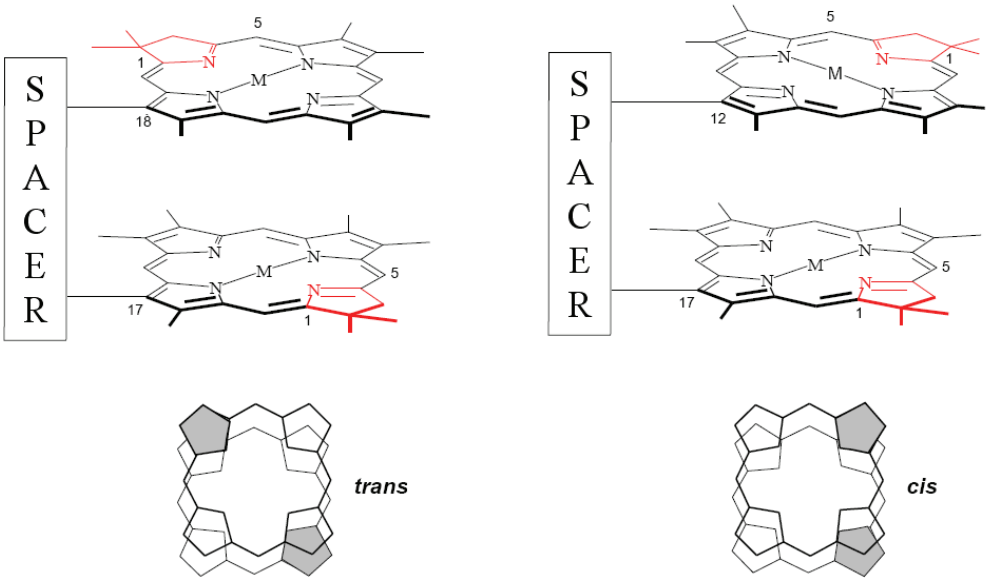
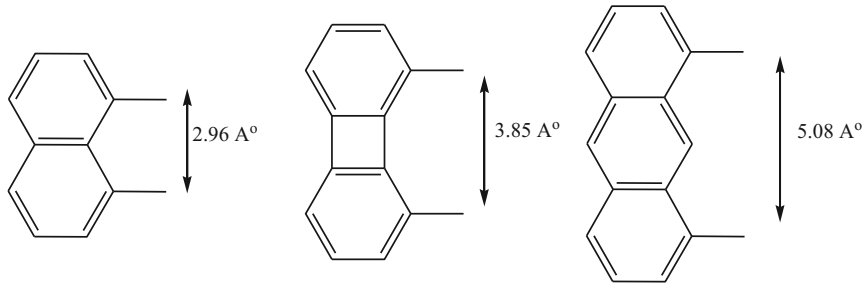


Figure 17: The cofacial chlorin dimer in different orientations[52]

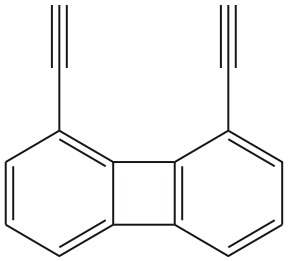
Inherent bacterial SP structure, the two BChl overlap partially at ring A. Accordingly in our designed model, two subunits were partially interfaced as well. The appropriate spacers for the chlorin dyads were also designed to reflect the natural system. Variation of the distances between two chlorins should be achieved by different spacers using polyarenes (Scheme 1).



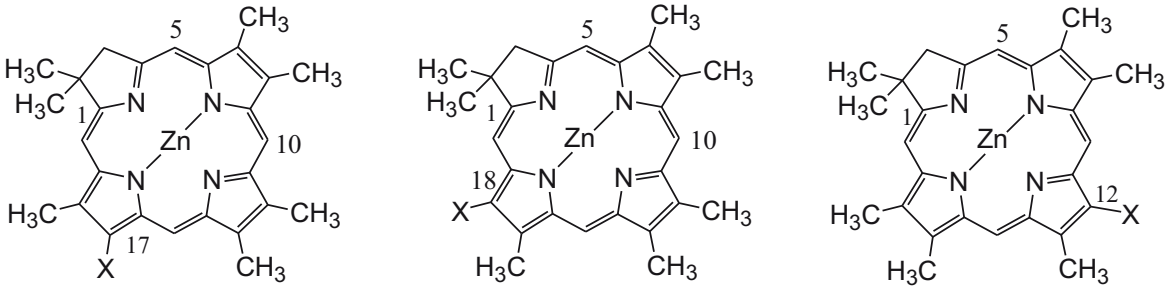
Scheme 1: Spacer variation

Scheme 1 indicates that a biphenyl unit could be the well-suited spacer with a distance of 3.85 Å comparable to the Bchl. dimer of the bacterial reaction center (3.2 Å) and the chlorophyll dimer in PS I (3.6 Å).

The coupling of chlorins to the spacer should be performed by the Shonogashira reaction which enables the connection between alkynyl functionalities of spacer with halide substitutions of chlorins. Therefore, the diethynylbiphenylen **10** was adopted as a spacer. Iodo or bromo substituted chlorins were envisaged as the subunits of the cofacial chlorin dimer (Scheme 2).



10



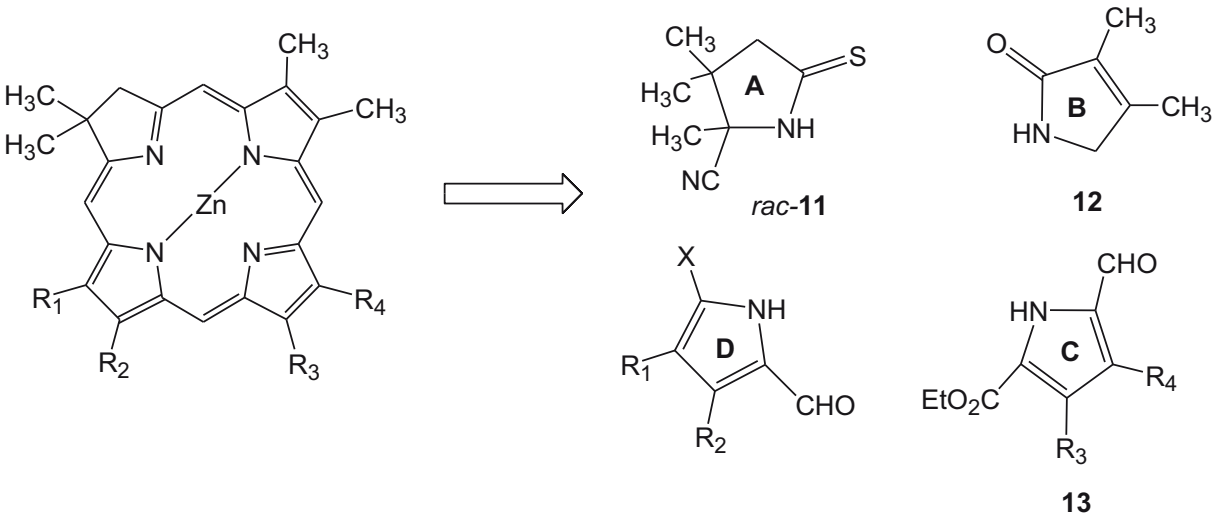
Scheme 2: Different subunits of envisaged chlorin dyads

The opposite *(trans)* chlorin dyad could be constructed by the combination of the 17-iodo or 17-bromochlorin with the 18- iodo or 18-bromo chlorin. The adjacent *(cis)* orientation should be formed by the combination of the 17-iodo or bromo chlorin with the 12-iodo or 12-bromochlorin.

2.2 STRATEGIES FOR SYNTHESIS OF COFACIAL CHLORIN DIMERS

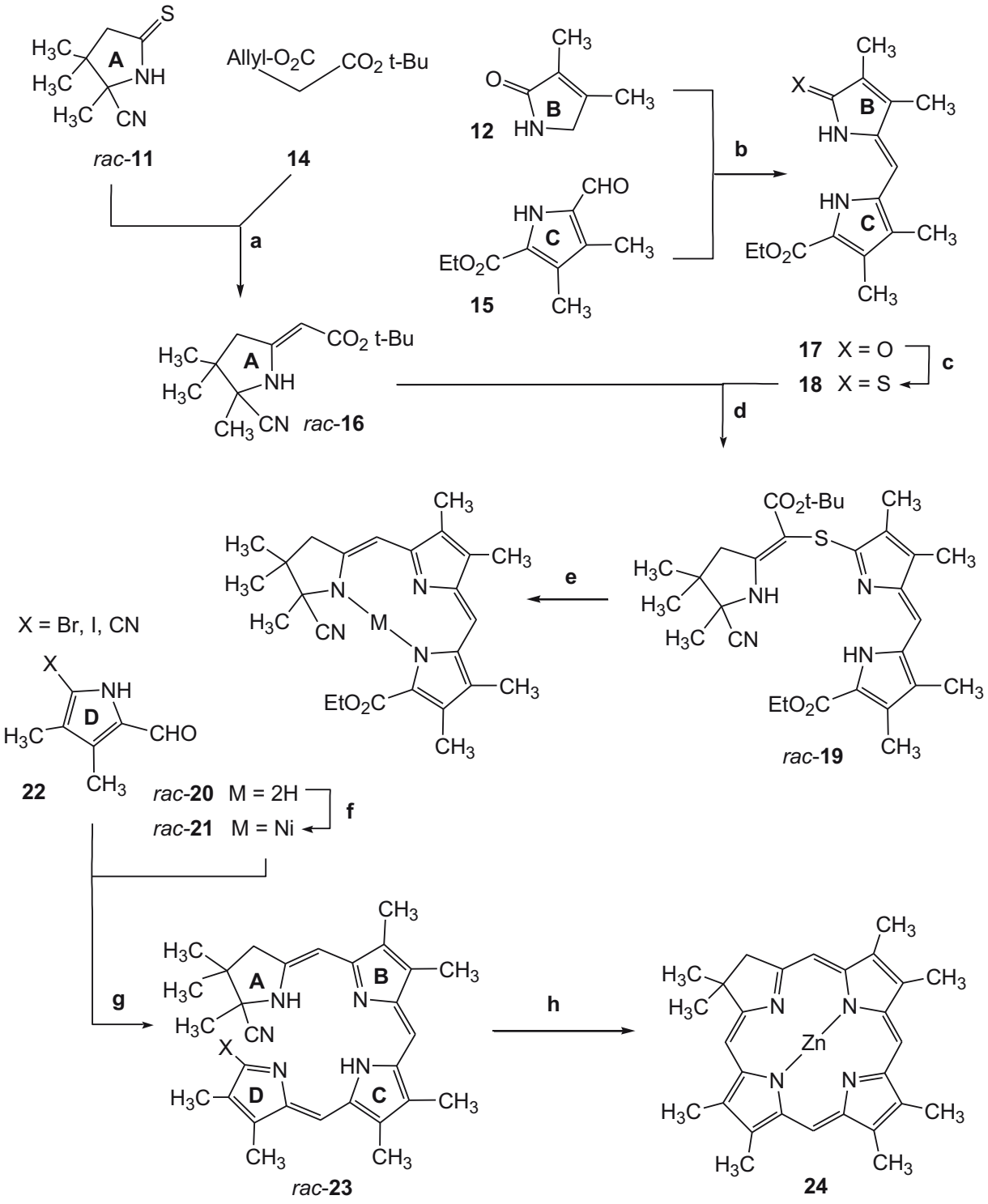
2.2.1 Concept for synthesis of geminally dialkylated chlorin subunits

The total synthesis of geminally dialkylated chlorin was developed according to a strategy of our laboratory making use of four heterocyclic building blocks (Scheme 3).[53-55] The preparative advantage is the great flexibility of the strategy. Any changes in the substitution pattern of the chlorin leading to different substituted chlorins can be introduced while the stage of heterocyclic building blocks and linking sequence were not changed.



Scheme 3: The synthesis concept leading to geminally dialkylated chlorin

The synthetic procedure is described in Scheme 4. The condensation of the nucleophilic 5-position of the pyrrolinone **12** with the pyrrolcarbaldehyd **15** is taken place first, followed by the thiolation of the lactam function. The resulting thiolactam is linked to ring A building block *rac*-**16** via a selective nucleophilic ester unit using the sulfide contraction method.[56] The formed tricycle is stabilized by complexation with nickel(II) yielding nickel tricycle *rac*-**21**. *Rac*-**21** can be condensed after the ester cleavage and decarboxylation with the pyrrolecarbadehyde **22** affording *rac*-**23**. The cyclization of secochlorin *rac*-**23** is carried out by base-induced or thermal HCN elimination to form chlorin **24**.

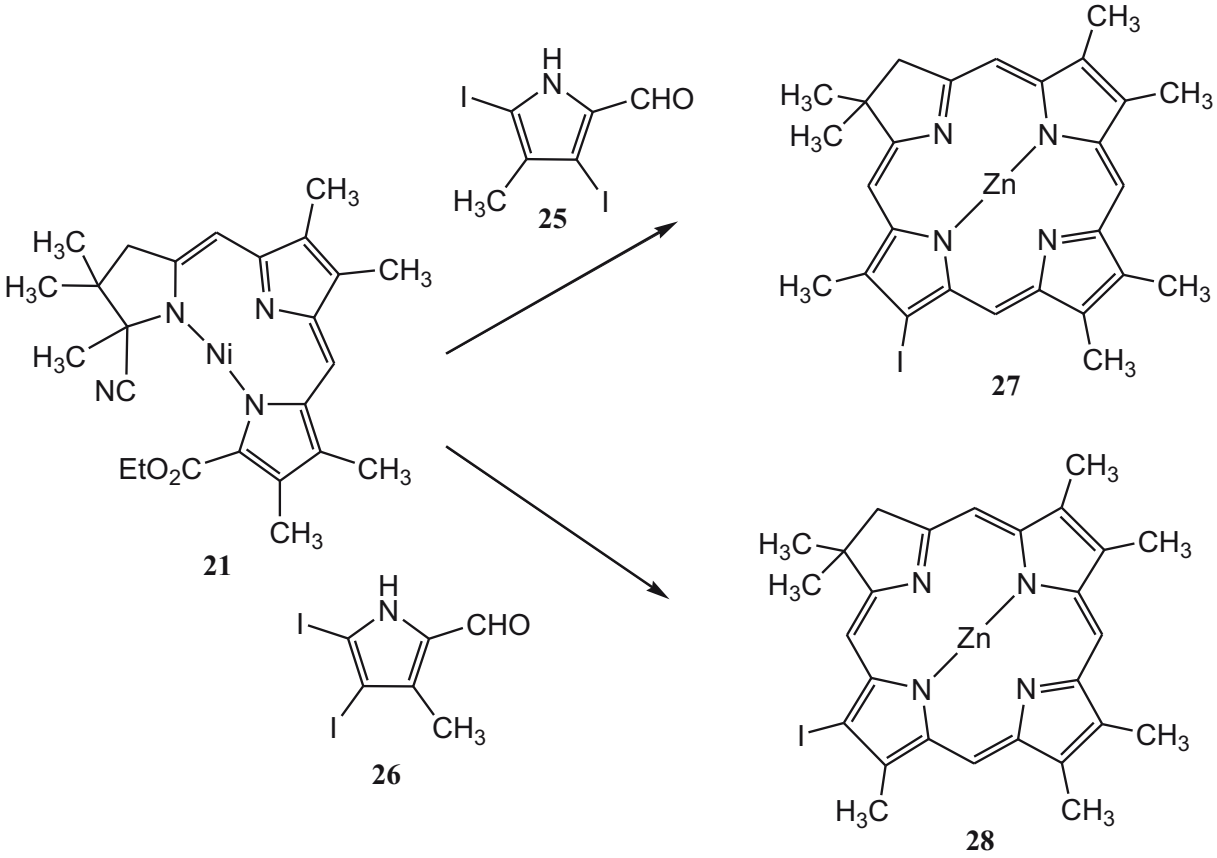


Scheme 4 : Synthesis of a geminally dimethylated chlorin **24**

a: 1.) CH_3CN, DBU, 20 min., 0 °C; 2.) $P(OEt)_3$, 80 °C, 2 h, $Pd(PPh_3)_4$, piperidine, THF*, reflux; **b**: DBU*, molecular sieve, benzene*, reflux, 16 h; **c**: Lawessons-Reagent, THF*, 40 °C; **d**: 1.) *rac*-**13**, NBS, CH_2Cl_2, rt., 20 min.; 2.) **17**, DBU, CH_3CN, rt., 40 min.; **e**: TFA, $P(CH_2CH_2CN)_3$, benzene, reflux, 20 min.; **f**: $Ni(OAc)_2.4\ H_2O$, NaOAc, $MeOH/CH_2Cl_2$, rt., 20 min.; **g**: 1.) THF, KOH, $MeOH/H_2O$ (9+1), reflux; 2.) *p*-TsOH, $CHCl_3$, reflux; 30 min.; **h**: 1) $Zn(OAc)_2.H_2O$, *t*-BuOK, *t*-BuOH, 70 °C; 2) 25 % HCl/CH_2Cl_2.

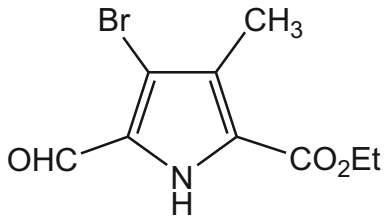
2.2.2 Concept for synthesis of iodinated geminally dialkylated chlorin subunits

Iodinated geminally dialkylated chlorins can be prepared using β-iodinated pyrrole building blocks. The tricycle *rac*-**21** can be condensed with the iodo substituted ring D building blocks followed by the subsequent cyclization during which different leaving groups at α position of rings D (I-, Br-, or CN-) and the cyano group of ring A are eliminated. Since iodide or bromide was substituted in the case of CN at the β position in ring D, a better yield of the resulting chlorins were achieved when α-leaving groups were bromide or iodide.[57] Therefore the ring D building block for the chlorin subunits of "*trans"*-chlorin dimer could be employed as 3,5-diiodo pyrrole **25** and 4,5-diiodo pyrrole **26**.

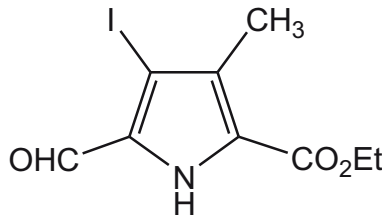


Scheme 5: The concept for synthesis of iodo chlorin **27**, **28**

Also the synthesis of 12-bromo or 12-iodo substituted chlorins could follow the concept of Scheme 4 using ring C pyrrole buiding block **29** or **30**.

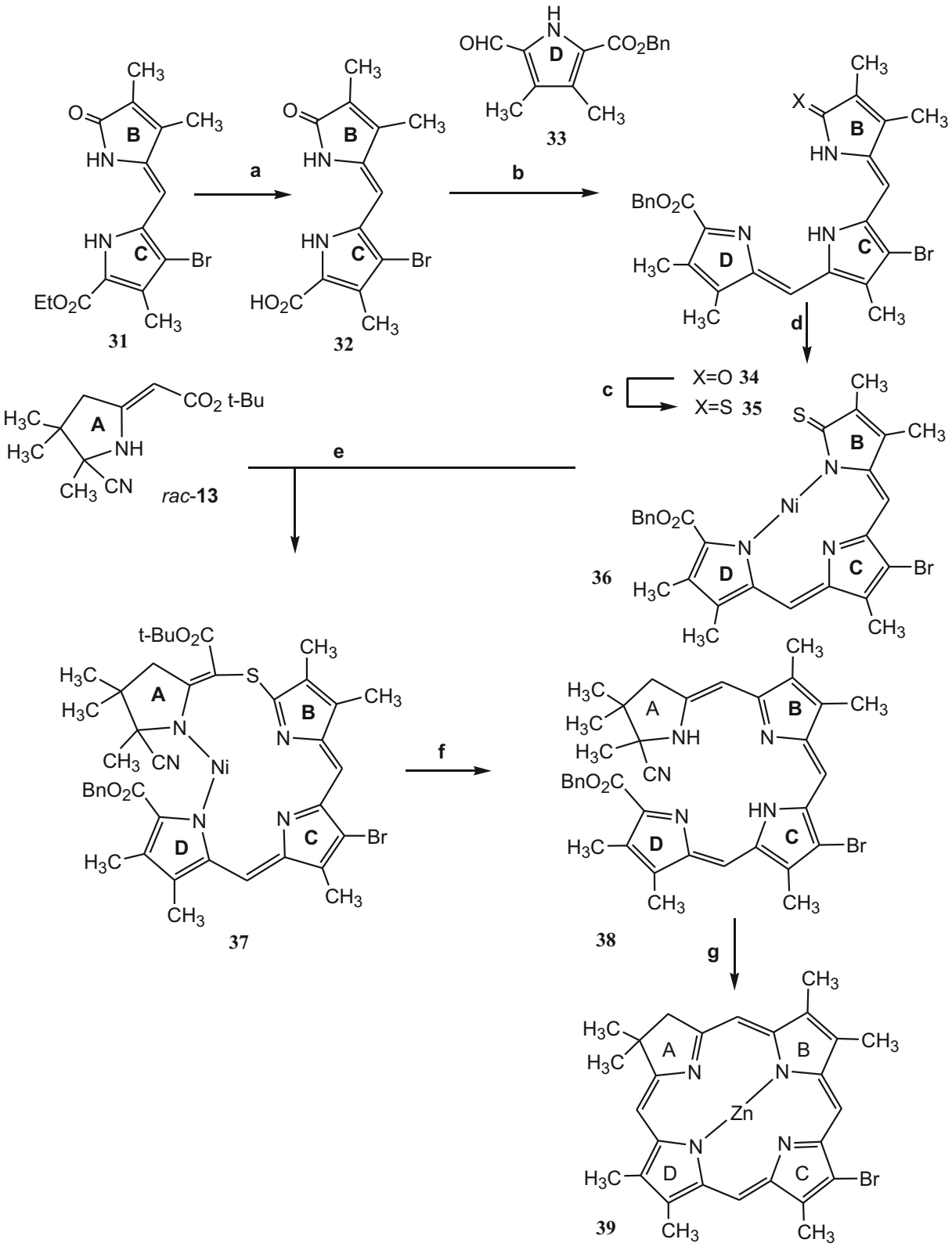


29



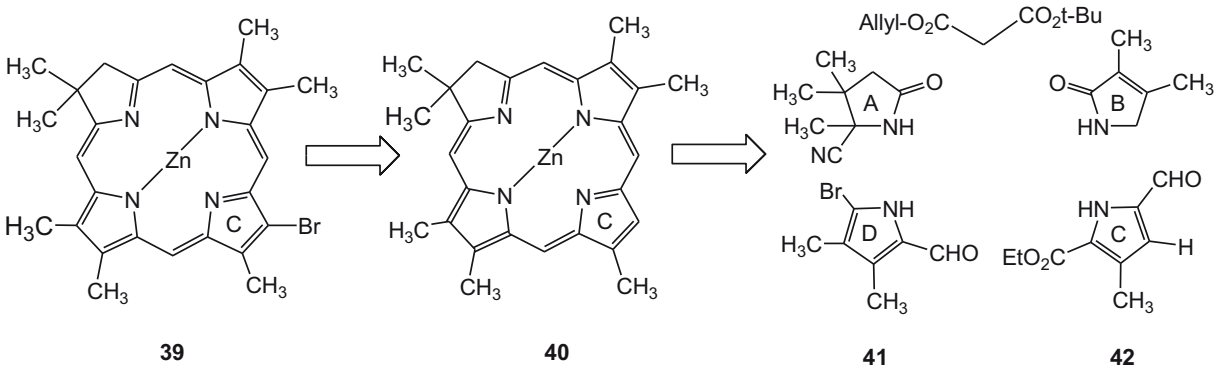
30

An alternative concept for the synthesis of 12-bromochlorin synthesis should be studied by changing the sequence of connection steps for obtaining the tetracyclic bilin intermediate **38**. The BC lactam bicycle **32** should be connected to ring D building block **33**. Subsequently, the resulting tripyrrin **36** should be linked with ring **A** *rac*-**13** to yield the bilin **38** via sulfur bridged tetracycle **37**. The cyclization following the usual scheme **4** could afford 12-bromochlorin **39** (Scheme 6).



Scheme 6: The modified sequence of the total synthesis of 12-bromochlorin **39**

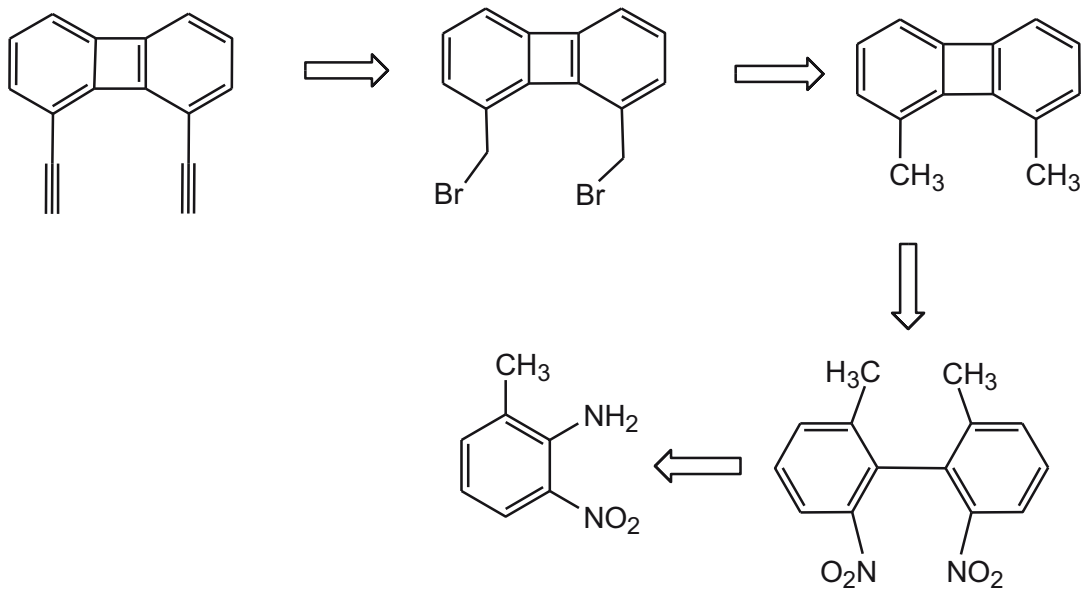
Another possibility for the preparation of 12-bromochlorin **39** synthesis should be performed by directed electrophilic bromination of 12-unsubstituted chlorin **40**. The starting chlorin **40** should be available from the coresponding monocyclic building blocks along the general route.



Scheme 7: Posibility of preparation of 12-Bromochlorin **39** by directed bromination

2.2.3 Concept for synthesis of a spacer subunit

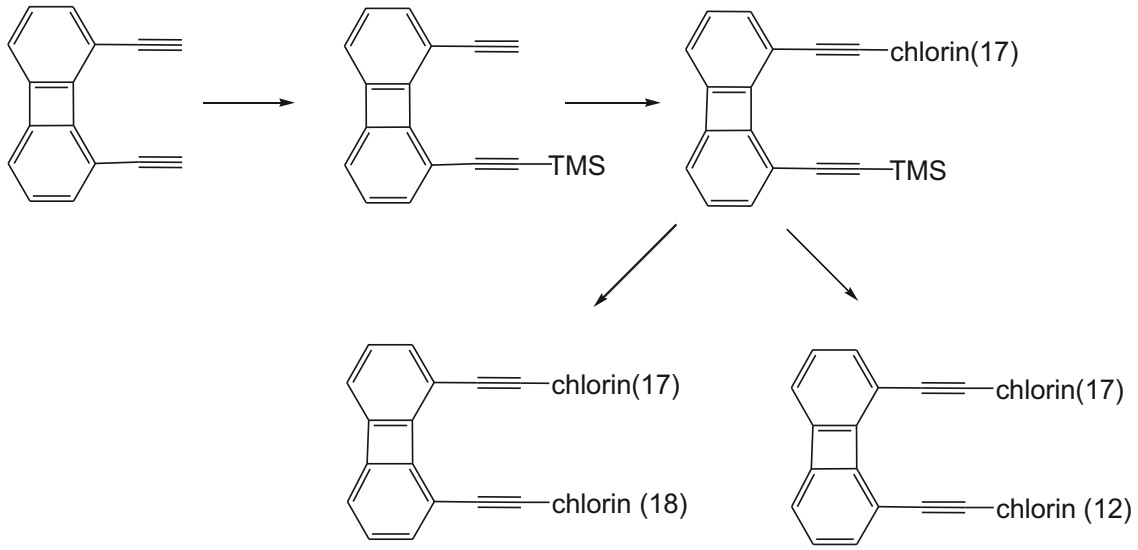
A synthetic approach leading to a diethynylbiphenylene spacer subunit was successfully developed in ourlabratory[58] starting from 2-methyl-6-nitro aniline (Scheme 8).



Scheme 8: Preparation of a diethynylbiphenylene spacer

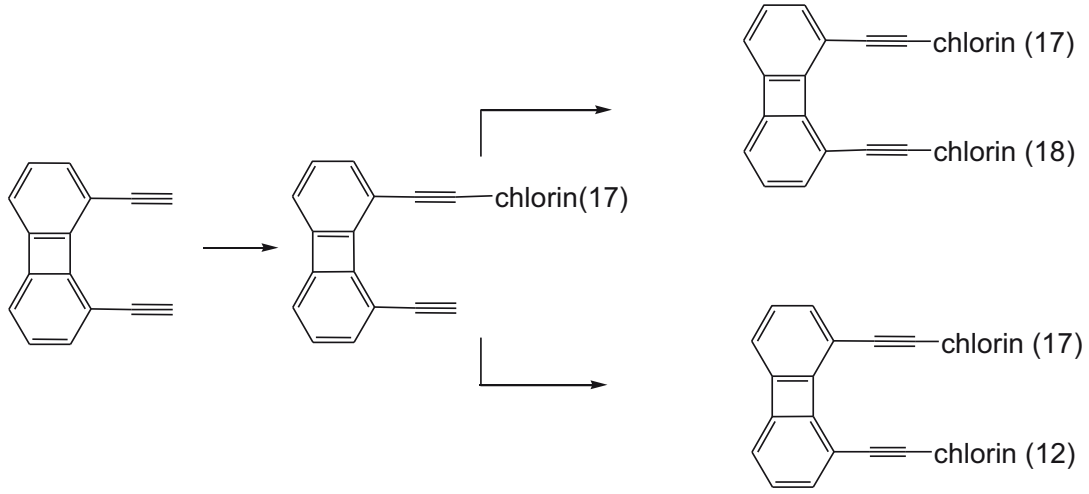
2.2.4 Construction of cofacial chlorin pairs from chlorin and spacer subunits

The linkage between chlorin and spacer should be performed by Shonogashira coupling. The selectivity should be achieved by protecting one of the acetylenyl functional groups by trimethylsilylane. After the connection of the first chlorin to the spacer, the protecting group should be deprotected in order to link another chlorin unit. The 17-iodo chlorin was selected as the first subunit because the resulting mono coupling intermediate could be used for the synthesis of both *cis*- and *trans*- arrangement (Scheme 9).



Scheme 9: Concept for the linkage sequence between chlorin and spacer subunits

Another concept of the SP synthesis is based on the dynamic control of some factors such as temperature, concentration of the reaction solution and the ratio of the starting material to afford the chlorin-spacer mono coupling product. The chlorin dyad could be achieved by the subsequent insertion of another chlorin.



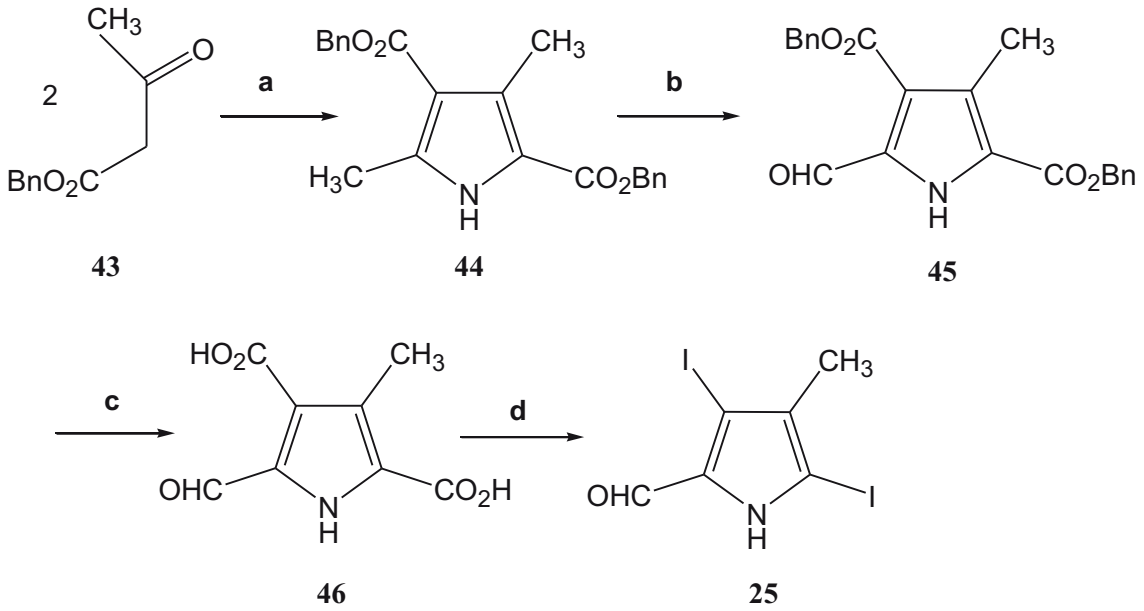
Scheme 10: Concept of the direct connection pathway between chlorin and spacer subunits

3. RESULTS AND DISCUSSION

3.1 PREPARATION OF IODO PYRROLE BUIDING BLOCKS

The synthetic approach to attain ring D subunits of the dialkylated iodochlorin has been previously developed in our research group.[52] The present work is aimed to optimize the synthesis procedure and prepare starting materials for the next tasks.

3,5-diiodopyrrole is the ring D building block of 17-iodochlorin **27** and it was obtained from the commercially available starting material, benzylacetoacetate **43,** which was converted to the pyrrole **44** by the Knorr reaction in high yield. Subsequently, the α-methyl group was oxidized by $Pb(CH_3COO)_4$ in order to produce the formyl pyrrole **45**. The hydrolysis of benzylester group leaded to the formation of the carboxylic acid. The decarboxylative iodination of the resulted pyrrole **46** yielded finally the diiodo formyl pyrrole **25** (Scheme 11).[59-61]

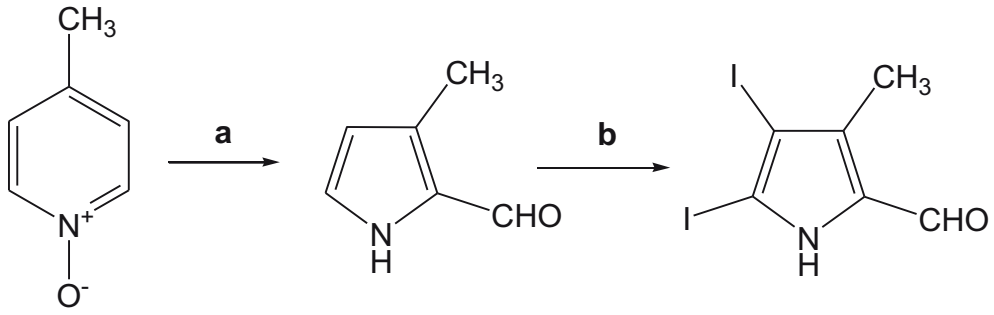


Scheme 11: Preparation of the ring D building block **25** of 17-iodochlorin **27**

a:$NaNO_2$, AcOH, 0 °C, Zn, reflux, 79.6 %; **b**: ammonium cerium(IV)nitrate, THF, water, AcOH, 2 h, rt., 65 %; **c**: 10 % Pd-C, H_2, quan.; **d**: $NaHCO_3$, I_2, KI, 20 min, 70 °C, 25 %.

As illustrated in scheme 12, γ-picoline-N-oxide **47** was rearranged to form formylpyrrol **49** by being exposed to a high intensive lamp in an aqueous copper sulphate solution.[62] The

iodination at two unsubstitued carbon position gave the 4,5-diiodpyrrol **26** as the ring D building block of 18-iodochlorin **28**.



47 **48** **26**

Scheme 12: Synthesis of the ring D building block **26** of 18-iodochlorin **28**

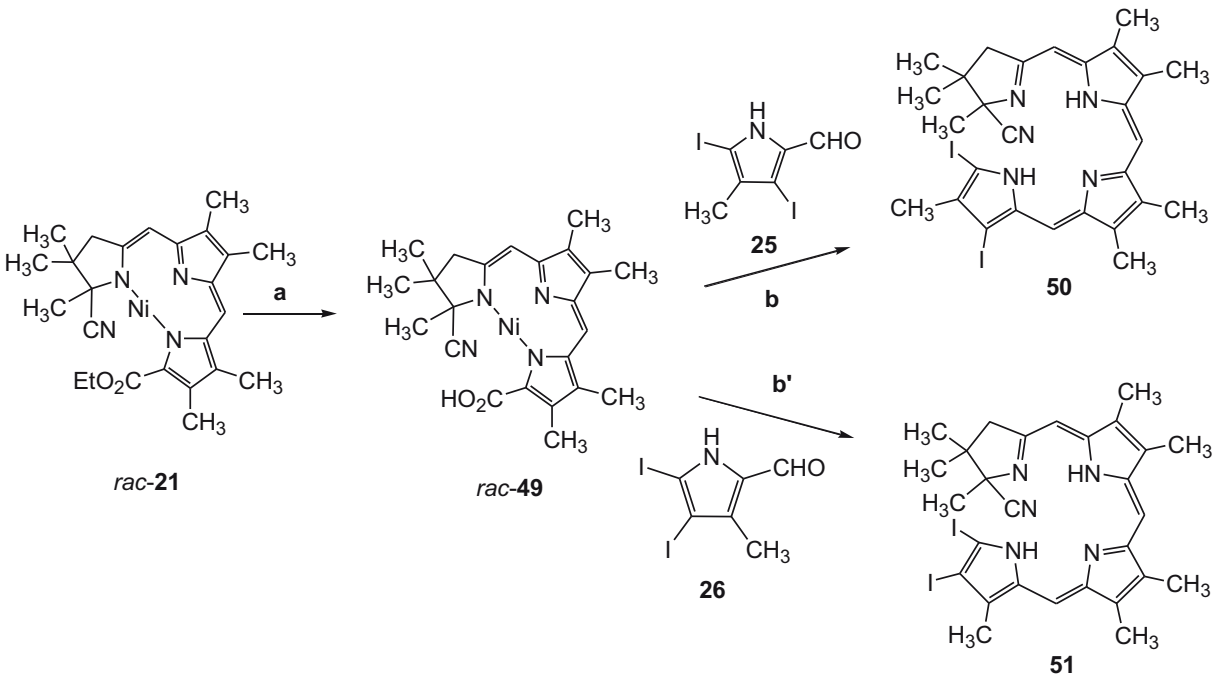
a: $CuSO_4$, H_2O, hυ, 40 h, rt., 13 %; **b**: DMF*, NaOH, I_2, 1 h, 40 °C, 39.5 %.

3.2 SYNTHESIS OF GEMINALLY DIALKYLATED CHLORINS WITH IODINE SUBSTITUENTS

The synthesis of 17- and 18-Iodochlorin followed the concept for chlorin synthesis (Scheme 4), making use of rings A, B, C and D building blocks.

The nickel tricycle *rac*.**21**, which was synthesized according to the process described in the section 2 (page 22), underwent the condensation pathway with the iodinated ring D building blocks **25**, **26** (Scheme 13).

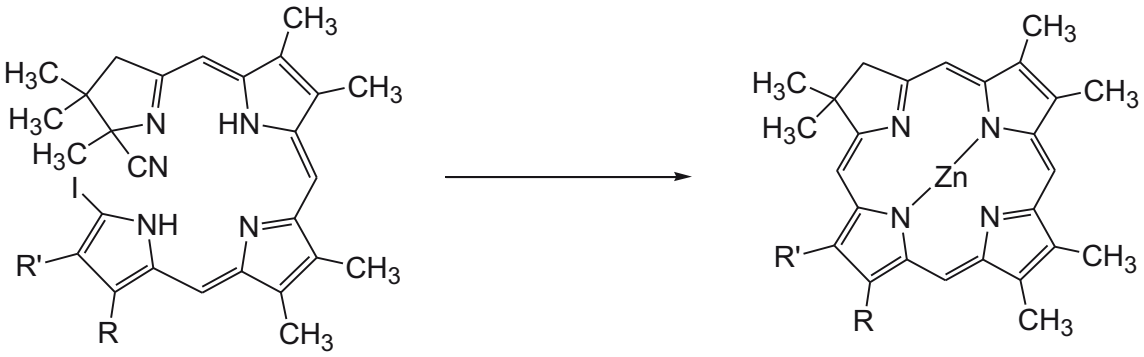
Hydrolysis of the ester function with methanolic-aqueous KOH solution produced the free carboxylic tricycle *rac*-**49**. Under acidic conditions, this tricycle was decomplexed and the α-aldehyde group of the ring D was activated by protonation. Subsequently, the tricycle underwent an nucleophilic attack on the α–position of ring C, followed by decarboxylation and rearrangement of the π-system establishing the tetracycles **50, 51**. To avoid decomposition of intermediate compounds, in this synthetic process, milder reaction conditions during the condensation were achieved by performing the reaction at room temperature and for a longer time (Scheme 13).



Scheme 13: Synthesis of the secochlorins **52**, **53**

a: KOH, MeOH/H_2O, THF, 70 °C, 30 min.; **b**: **25,** $CHCl_3$, p-TsOH, rt., 16 h, 67 %, **b'**: **26**, $CHCl_3$, p-TsOH, rt., 16 h, 62 %.

The recomplexation and cyclization of the tetracycle was performed under basic reaction condition.



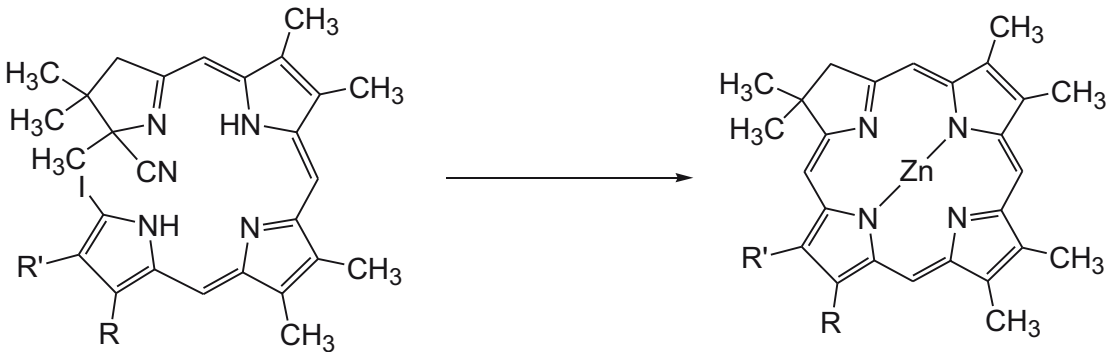
50: R: I, R': CH_3
51: R:CH_3, R': I

27: R: I, R': CH_3
28: R:CH_3, R': I

Scheme 14: Cyclization of tetracyclic bilins to chlorins **27**, **28**

DBU, sulfolane*, $Zn(OAc)_2$, 3 h, 80 °C, ~79 %.

In presence of zinc(II) acetate, the zinc complex of tetracycle was formed. The initial step of the cyclization started with the elimination of HCN leading to the formation of an enamine double bond at ring A, which subsequently attacked iodide substitution at α-position of ring D. The HI elimination then closed the π-system of the chlorin (Scheme 14).[63]
Other approaches for cyclization were performed in another basic solvent system of *tert*-BuOH/BuOK or by thermal cyclization. However, in all cases, the yields did not exceed 10 % due to the decomposition of intermediate products (Scheme 15).



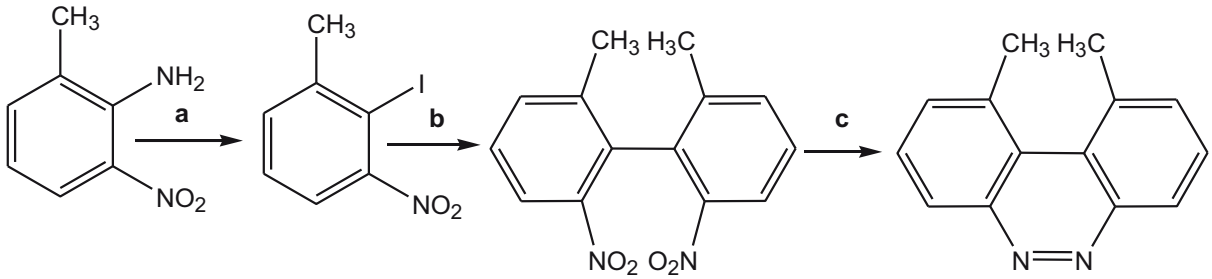
Scheme 15: Studies on alternative cyclization conditions

tert-BuOH/tert-BuOK, $Zn(OAc)_2$, reflux, 2 h.
1: $Zn(OAc)_2$, MeOH, 20 min., rt., **2**: 1,2,4-triclobezene, 210 ^{o}C, 45 min., ~10 %.

3.3 SYNTHESIS OF DIETHYNYLBIPHENYLEN SPACER SUBUNIT

The implementation of the biphenylene **10** synthesis as the spacer subunit was basically conducted according to Thorsten Könekamp's dissertation,[58] Wilcox *et al.* and Collman *et al.* .[64,65]

Starting from the commercially available 6-methyl-2-nitroaniline **52**, the corresponding iodo substituted benzene **53** was formed by Sandmeyer reaction. The Ullmann coupling linked two iodobenzenes to form the dinitrobiphenyl **54**. Subsequently, the reduction of **54** by $LiAlH_4$ afforded dimethylbenzo[c]cinnoline **55** (Scheme 16).

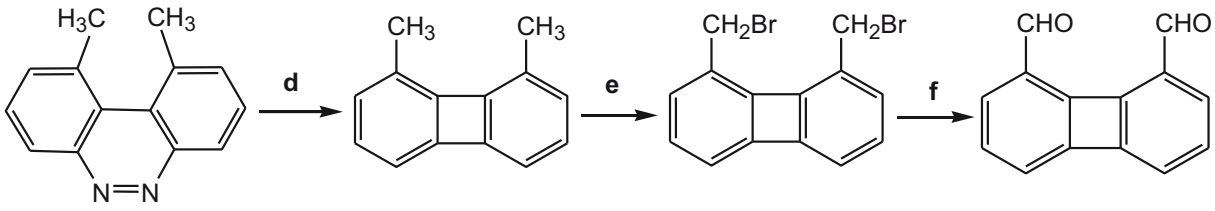


52 **53** **54** **55**

Scheme 16: Synthesis pathway of benzo[c]cinnoline **55**

a: 1) HCl, $NaNO_2$, 0 °C, 30 min.; 2) KI, 10 min., (90.4 %); b: DMF, Cu, reflux, 6 h, (61.6 %);
c: $LiAlH_4$, benzene, diethylether, 2 h, 62 %.

The synthesis of 1,8-dimethylbiphenylene **56** from dimethylbenzo[c]cinnoline **55** based upon a pyrolysis reaction has been described by Wilcox *et al.*.[64] After adjustment of several experimental parameters (e. g. apparatus geometry, pyrolysis temperatures and reaction time), the sufficient pyrolysis procedure was established at 700 °C with 2 g scale of starting material **55** for 1 hour of the reaction time. Subsequently, the radical bromination with N-bromo-succinimide, under light irradiation, gave bis(bromomethyl)biphenylene **57** in 35 % yield because monobromobiphenylene was also formed as the major side product. The following oxidation of bis(bromomethyl)biphenylene **57** yielding diformylbiphenylene **58** was achieved by using tetra-*n*-butyl ammonium dichromate as an oxidation reagent (Scheme 17).

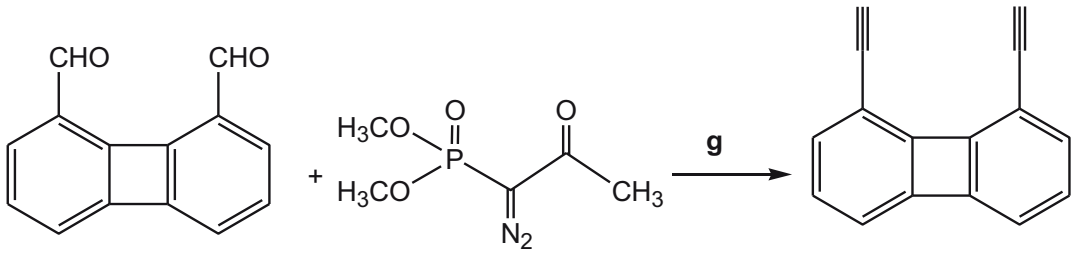


55 **56** **57** **58**

Scheme 17: preparation of diformylbiphenylene **58**

d: Pyrolysis, 700 °C, 1 h, (27.9 %); **e**: NBS, dibenzoylperoxid, CCl_4, hν (150 W), reflux, 6 h. (35 %); **f**: $((n\text{-}Bu)_4N)_2Cr_2O_7$, $CHCl_3$, reflux, 3 h., (78 %).

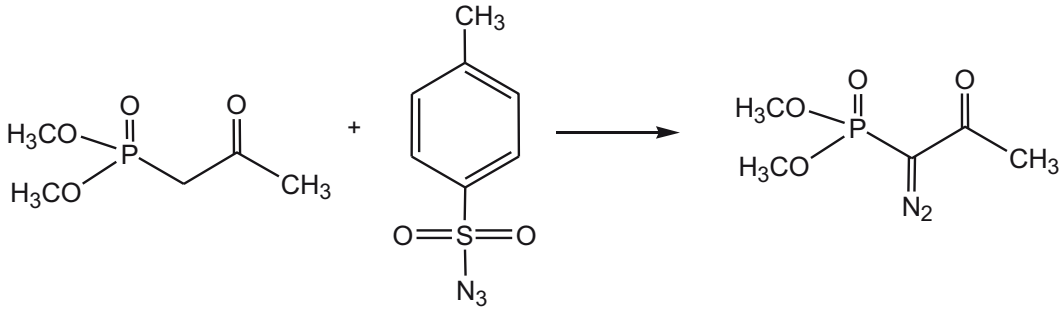
As represented in schemes 18 and 19, the functional ethynyl group of the spacer **10** was introduced by the Seyferth-Gilbert homologation of diformylbiphenyl using Bestmann'reagent. The preparation of the Bestmann's reagent **59** was performed by the diazo transfer of *p*-toluolsulfonylazide to dimethyloxopropylphosphonate.[66]



58 **59** **10**

Scheme 18: Seyferth-Gilbert homologation of diformylbiphenylene **58**

g: K_2CO_3, MeOH, rt., 4 h, (80.1 %).



60 **61** **59**

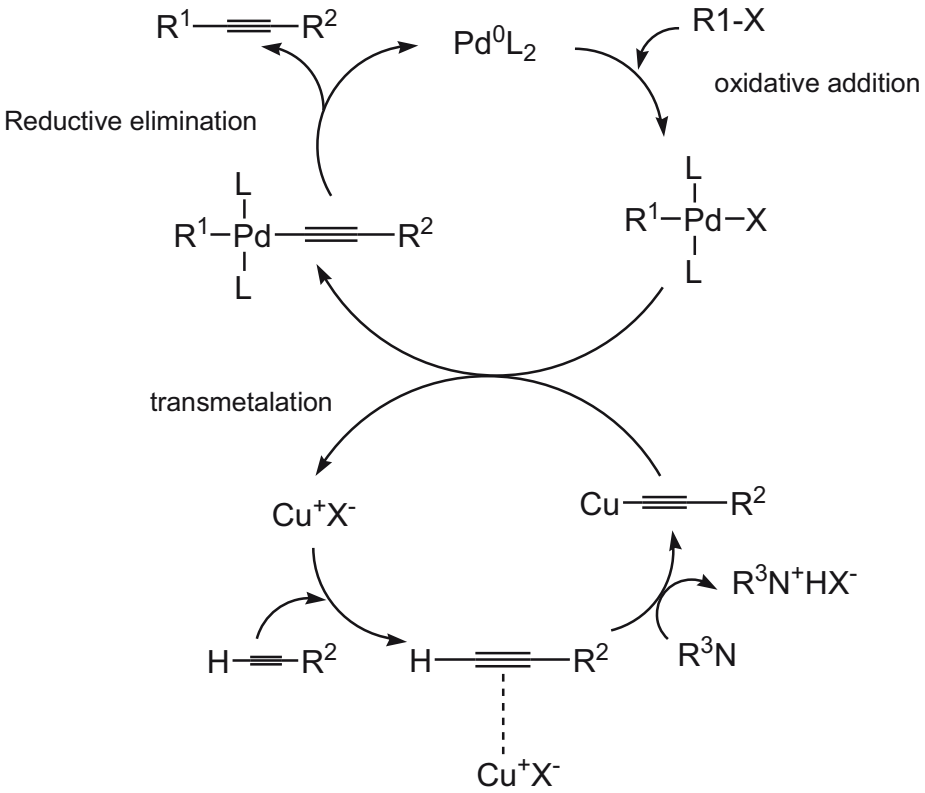
Scheme 19: Preparation of Bestman's reagent

K_2CO_3, H_3CCN, rt., (82.7 %).

3.4 SYNTHESIS AND STRUCTURAL CHARACTERIZATION OF A COFACIAL CHLORIN DIMER

The connection of 18-iodochlorin with the spacer was performed by the Shonogashira reaction.[67-71] This refers to the sp^2-sp coupling between the terminal alkyne and an aryl halide in the presence of Pd(II)/Pd(0) catalyst, with or without Cu(I), under basic conditions.

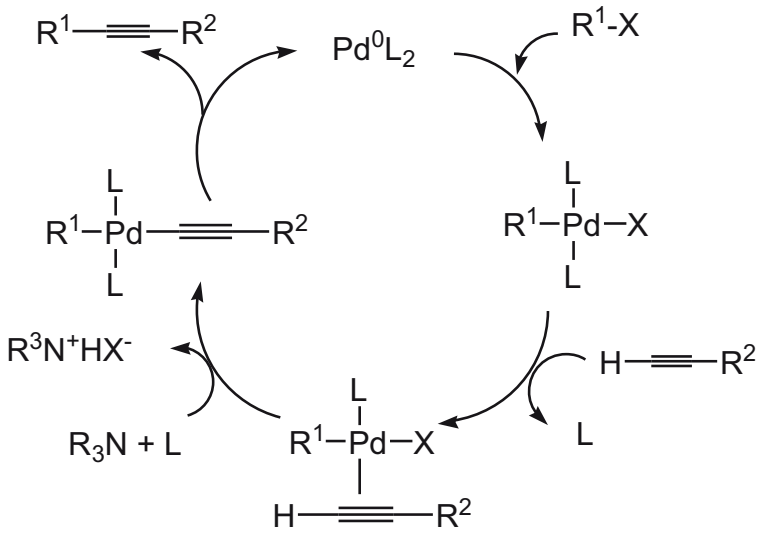
Scheme 20 describes the initial mechanism including key elements: oxidative addition, transmetalation and reductive elimination. In the course of the oxidative addition, Pd^0L_2 is inserted into the carbon-halogen bond of RX to form the square-planar complex PdL_2R^1X. In the next step, the Pd-cycle connected with the cycle of the copper cocatalyst (the Cu-cycle) (Scheme 20). Thus, the transmetalation of the copper acetylide occurring in the Cu cycle generates the $R^1PdR^2L_2$ complex, which then undergoes a *trans-cis* isomerization. The last step of the reductive elimination gives the final coupled R^1-C≡C-R^2 and releases palladium(0) complex, starting a new catalytic cycle.



Scheme 20: The mechanism of the copper-cocatalyzed Sonogashira reaction

The mechanism of copper-free Sonogashira reactions is still under debate. The first step should be the oxidative addition of R^1-X to the palladium(0) complex to form $PdXL_2$. The

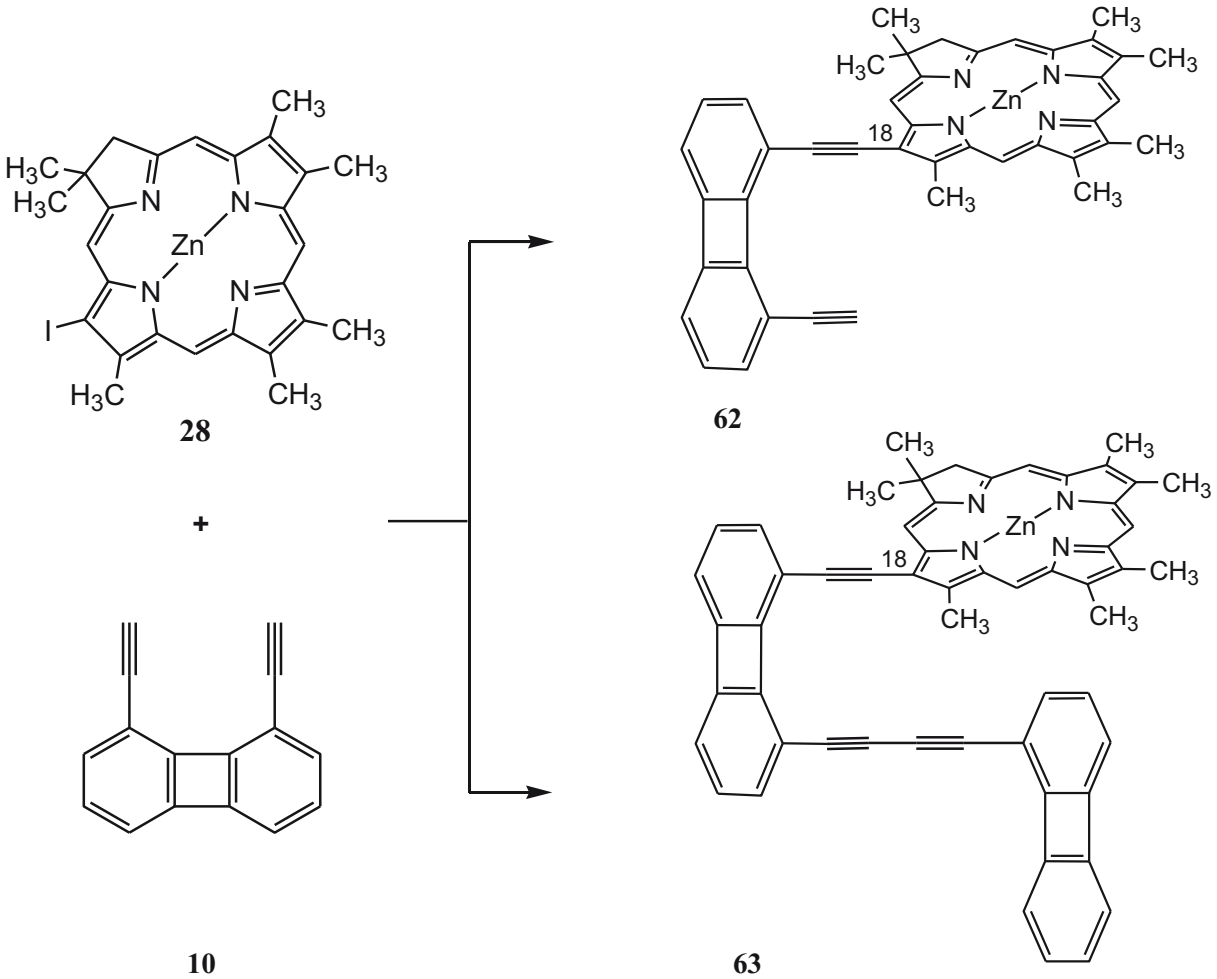
complexation of the alkyne to the complex is supposed to be firstly proceeded with the displacement of one ligand to give the intermediate complex $PdXLR^1(HR^2)$. The bonded alkyne would be easily deprotonated by an amine, forming the new complex $R^1Pd\text{-}PdL_2R^1R^2$, which gives the coupling product $R^1\text{-}C{\equiv}C\text{-}R^2$ by reductive elimination (Scheme 21).



Scheme 21: The mechanism of copper-free Sonogashira reaction

The catalyst for the Shonogashira reaction was developed mostly based on palladium-phosphine ligand complex with or without the presence of copper(I) salt, in the presence of amine. Among various reaction conditions frequently performed,[68-70] the ratio of the catalyst would be up to 5 mol %, the solvents could be DMF, toluene, THF, and the amines could be TEA or pyrrolidine. To avoid the Glaser-type homocoupling, the strict exclusion of oxygen was also required.[70,71]

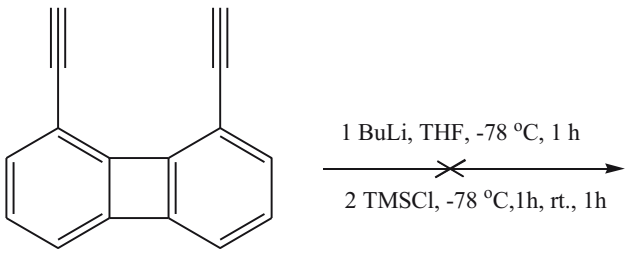
Some reaction conditions were tested for the coupling of iodochlorins with the spacer, such as $Pd(dba)_2$ and P(*o*-tol)$_3$, $Pd[PPh_3]_4$/CuI, Pd(dba) and As(*o*-tol)$_3$, in different solvents namely THF, DMF and toluene, as well as applying different reaction times. As the result, the best condition was found with $Pd(dba)_2$ and P(*o*-tol)$_3$ in toluene/TEA (5:1). Unfortunately, side products were observed decreasing the yield of this reaction. The tetraphenyl-chlorin **63** as one of side products resulted from the monochlorinspacer homocoupling was identified by MS spectra (Scheme 22).



Scheme 22: Synthesis of the monochlorin-spacer unit **62** and the formation of side product **63**

$Pd_2(dba)_3.CHCl_3$, P(o-tol)$_3$, Toluene/TEA (5:1), 60 ^oC, 7 h,~10 %

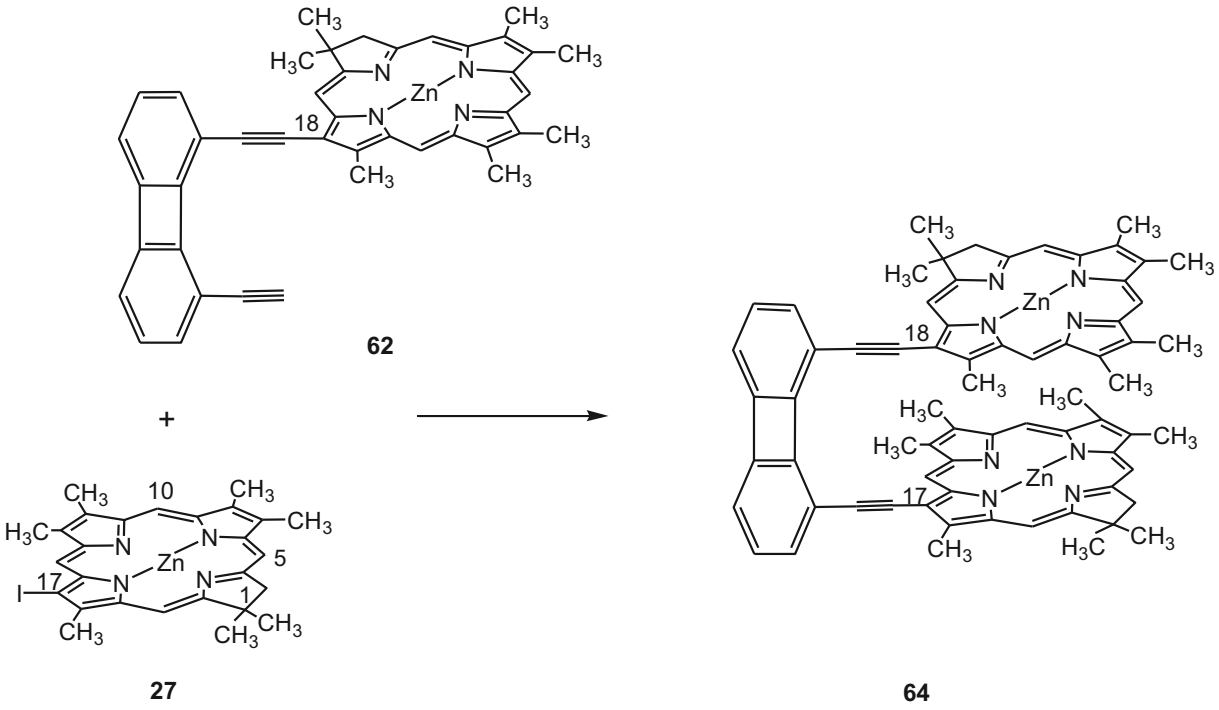
To avoid the homocoupling and to optimize the desired coupling reaction, as illustrated in scheme 13, the spacer could be protected by a trimethylsilane group,[72] following the original concept (page 24). However, the attempt of lithiation, followed by quenching with TMSCl was not successful.



Scheme 23: Attemp to protect the spacer's functional side

The final step of the total synthesis of chlorin dyad was the coupling of the 17-iodochlorin **27** with the mono chlorin-spacer **62**. This reaction was performed under the same reaction

conditions but for a longer reaction time (Scheme 24).



Scheme 24: Synthesis of chlorin dyad **64**

$Pd_2(dba)_3.CHCl_3$, $P(o\text{-}tol)_3$, Toluene/TEA (5:1), 60 °C, 17 h, ~10 %.

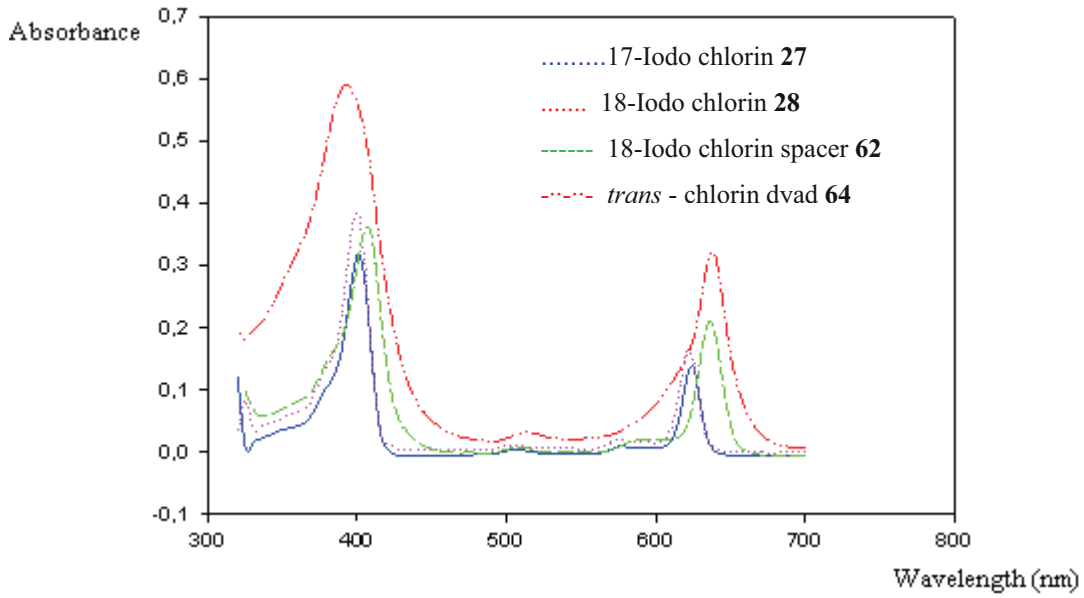


Figure 18: UV-VIS spectra of the *trans*-chlorin dyad **64**, monochlorin-spacer **62** and chlorin subunits **27**, **28**

The UV spectra presented in figure 18 shows the red shift of the Q bands of chlorins **27**, **28**, monochlorin-spacer **62** and chlorin dyad **64** ranging from 625 to 635 and 640 nm respectively

due to the increasing the π-system. The double intensity of chlorin dimer **64** in the UV spectra compared to single chlorin reflexs the dimeric structure.

After excited at 400 nm, monochlorin-spacer **62** and chlorin dyad **64** showed high intensities of emission fluorescence at 638 nm while no fluorescence was observed in the case of chlorin **28** (Fig. 19). The broad band in the UV and the split of the Q-band in fluorescence spectra of chlorin dyad indicates the existence of two conformations of the dyad.

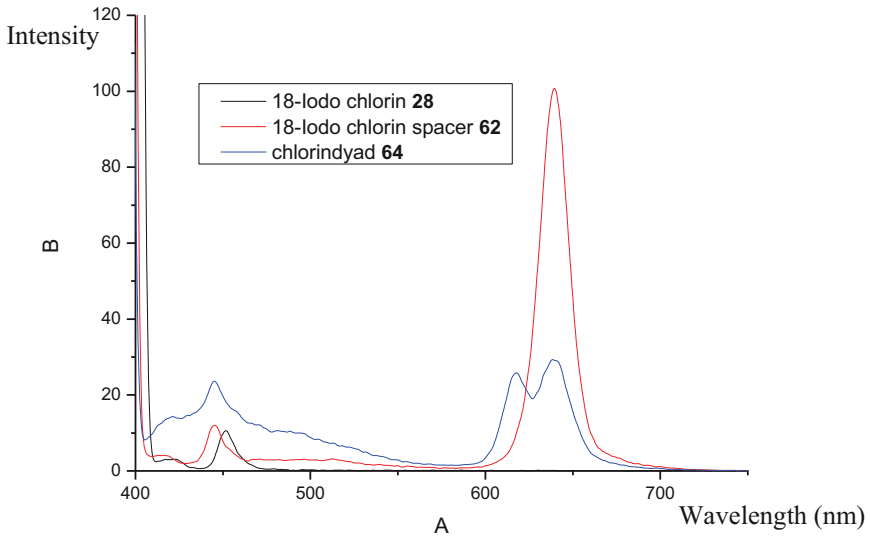


Figure 19: The Fluorescence of *trans*-chlorin dyad, monochlorin and chlorin subunits (10^{-6} M)

The conformation of the cofacial chlorin dimer was calculated based on semi-empirical PM3 calculations. The chlorin subunits of the dyad are arranged in two conformations. The energy for both conformations is almost equal with a caculated difference of only 1.5 kcal/mol. When looking perpendicularly at the chromophore plane, for structure **I**, two chlorin subunits are almost eclipsed to each other while for structure **II**, the chlorin subunits are only partially overlapping. The shortest distance between the two chlorin planes is about 3.2 Å while for the distance between two central Zn atoms it is about 4.5 Å. In both cases, the spatial separations of the two subunits are relatively close to those of SP in bacteria and plants, as shown in Fig. 3. The geometric orientation and the overlapping π-electron system of the conformation II are arranged remarkably similar to SP in P700 of plant reaction center. However, in order to confirm the electron transfer ability of this chlorin dyad, experimental and theoretical investigations are necessary in particular under the influence of an electron acceptor.

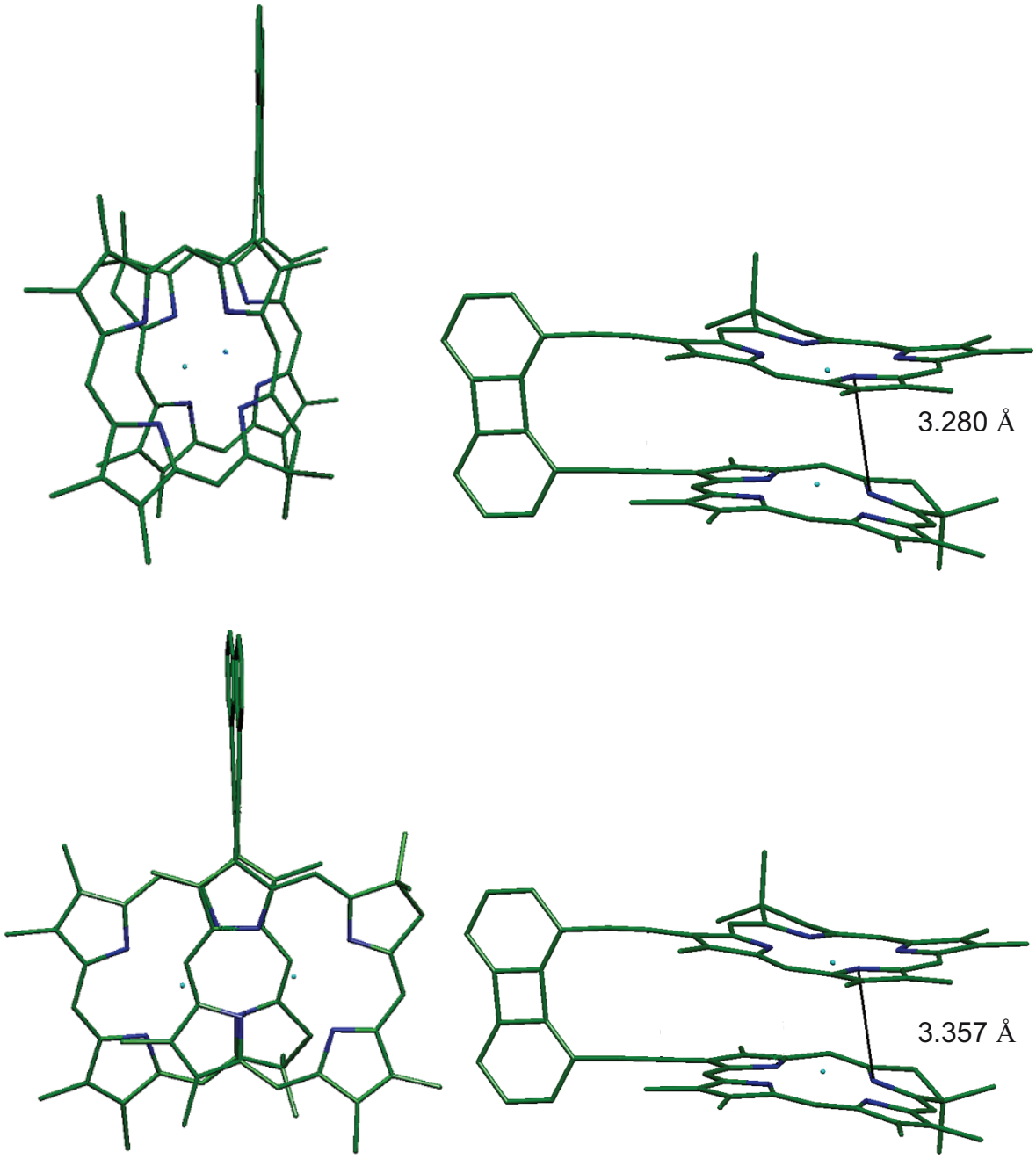


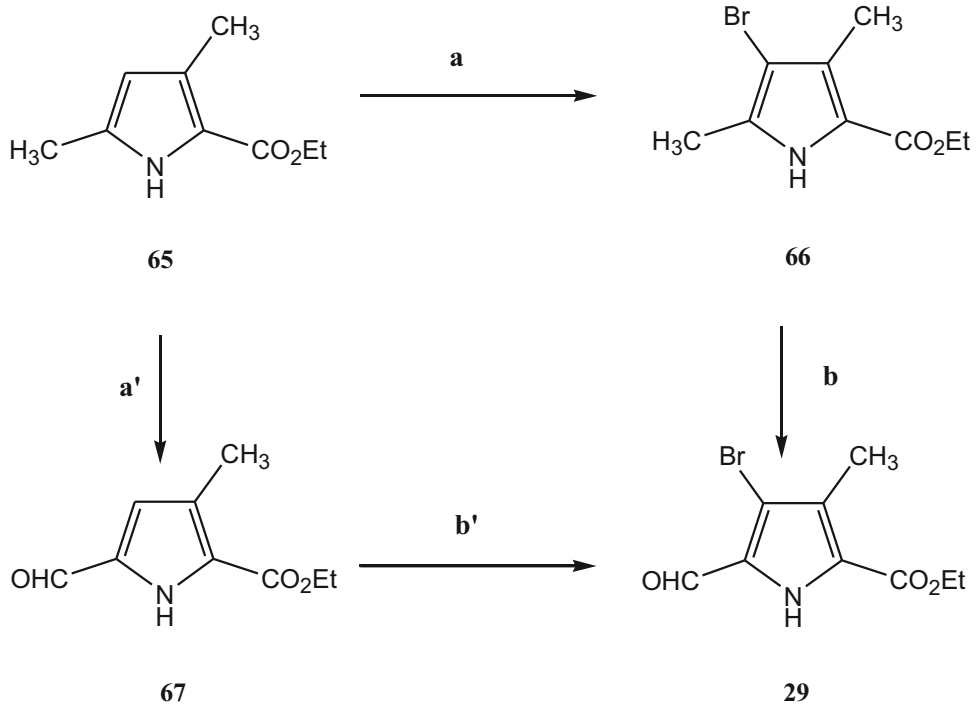
Figure 20: Top and side view of the cofacial chlorin dyad **I** and **II**

3.5 STUDIES DIRECTED TO SYNTHESIS OF 12-BROMO-2,2,7,8,13,17,18-HEPTALMETHYL CHLORIN

3.5.1 Synthesis of a bicyclic thiolactam

For the synthesis of 12-halide chlorin, pyrrole **29** or **30** (see 2.2.3) was employed. The more stable bromo BC building block compared to the iodo BC fragment should avoid halogen loss from the lactam.

The preparation of bromo pyrrole **29** as the ring C building block for 12-bromochlorin was carried out along two different pathways (Scheme 25). Both included bromination and oxidation. The bromination followed by oxidation procedure (a, b) gave a better yield than the alternative procedure with an interchange of the reaction steps (a', b').[73-76]

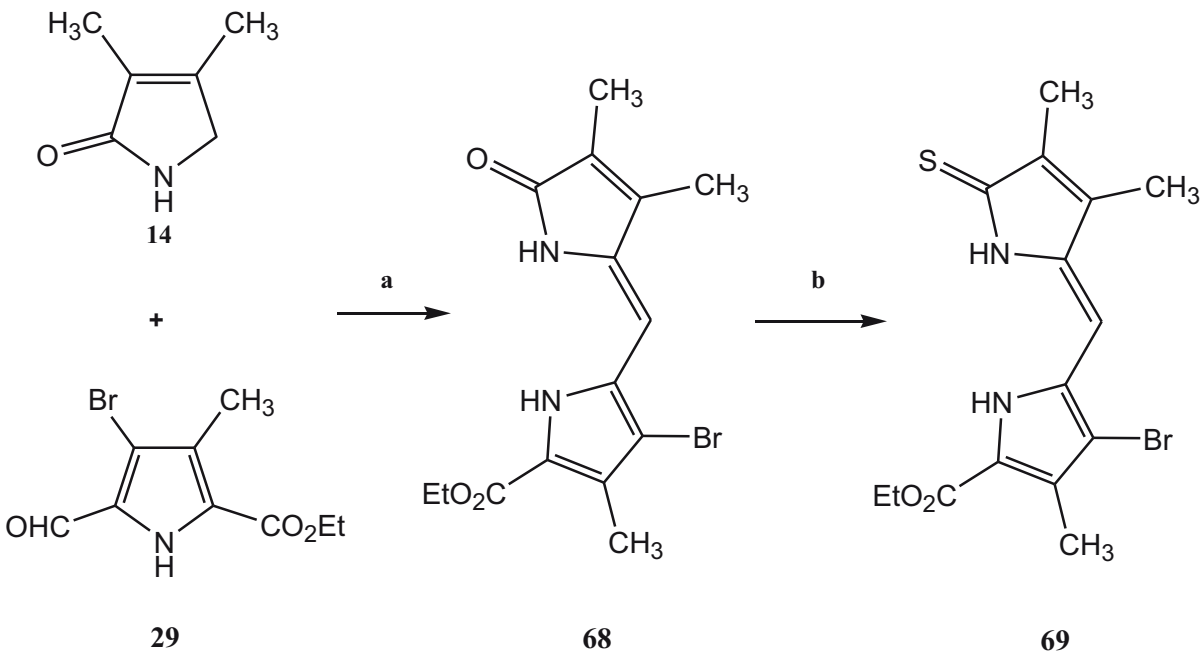


Scheme 25: Preparation of ring C building block **29**

a: NBS, -78 °C, 2 h, 70.2 %; **b**: **1**: $Pb(CH_3COO)_4$, 17 h; **2**: HCl 2.5 M, 4 h, 62.3 %.

a': $Pb(CH_3COO)_4$, 17 h; **2**: HCl 2.5 M, 4 h, 62 %; **b':** NBS, -78 °C, 2 h, rt., 3 h, 12 %.

Base-catalyzed condensation of pyrrolinone **14** and aldehyde **29** produced the bicyclic lactam **68** without any removal of bromide. **68** was then converted to the thio analogue **69** (Scheme 26).



Scheme 26: Synthesis of the bromo-substituted thiolactam **69**

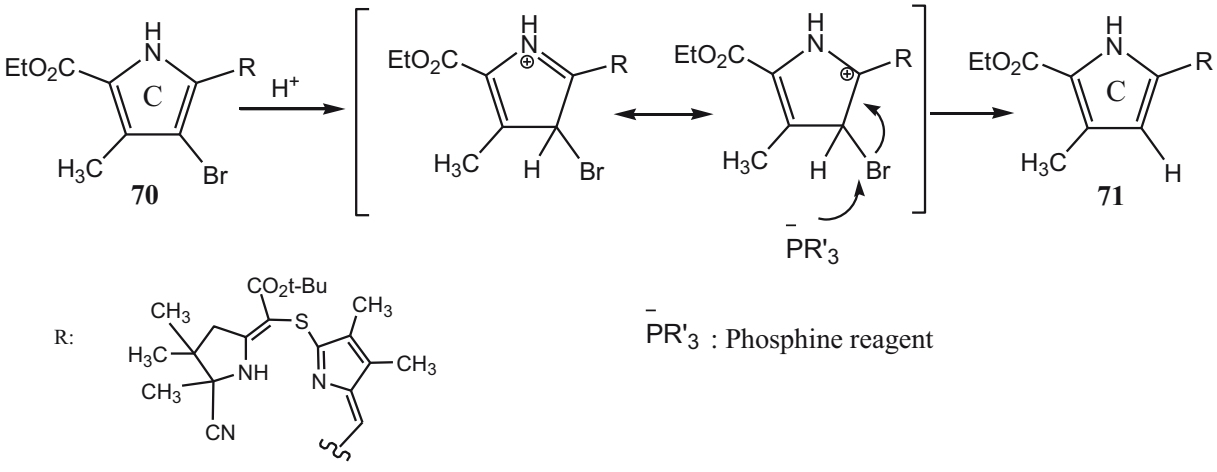
a: Schwesinger base, molecular sieve, benzene*, reflux, 15 h, (32.9 %);

b: Lawesson's Reagent, THF*, 40 °C, 3 hours, 72.5 %.

3.5.2 Synthesis of a tricyclic nickel complex

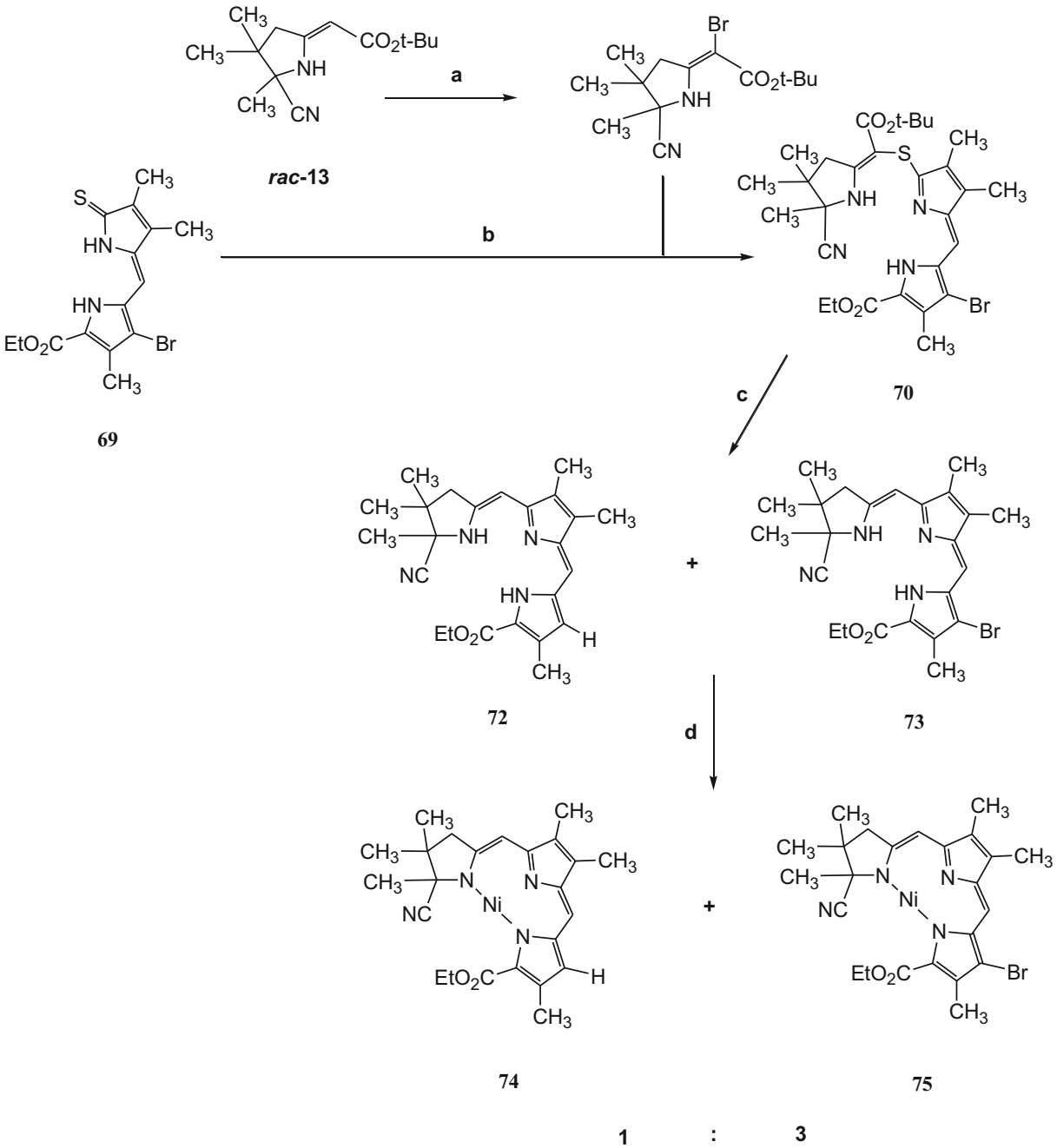
Coupling of brominated *rac*-**13** with thiolactam **69** yielded the tricyclic sulfide **70** (Scheme 29). In the further sulfide contraction step, under acidic conditions, the desired tricyclic **73** was formed togetther with by product debrominated tricycle **72**.

The bromide removal took place along with the sulphide contraction of **70** using $P(CH_2CH_2CN)_3$ in the presence of TFA. The bromide could be replaced by nucleophilic attack of the phosphine at the bromine yielding the brominated phosphorous (Scheme 27).



Scheme 27: Possible mechanistic course of unexpected bromide removal at ring C building block in the sulfid contraction

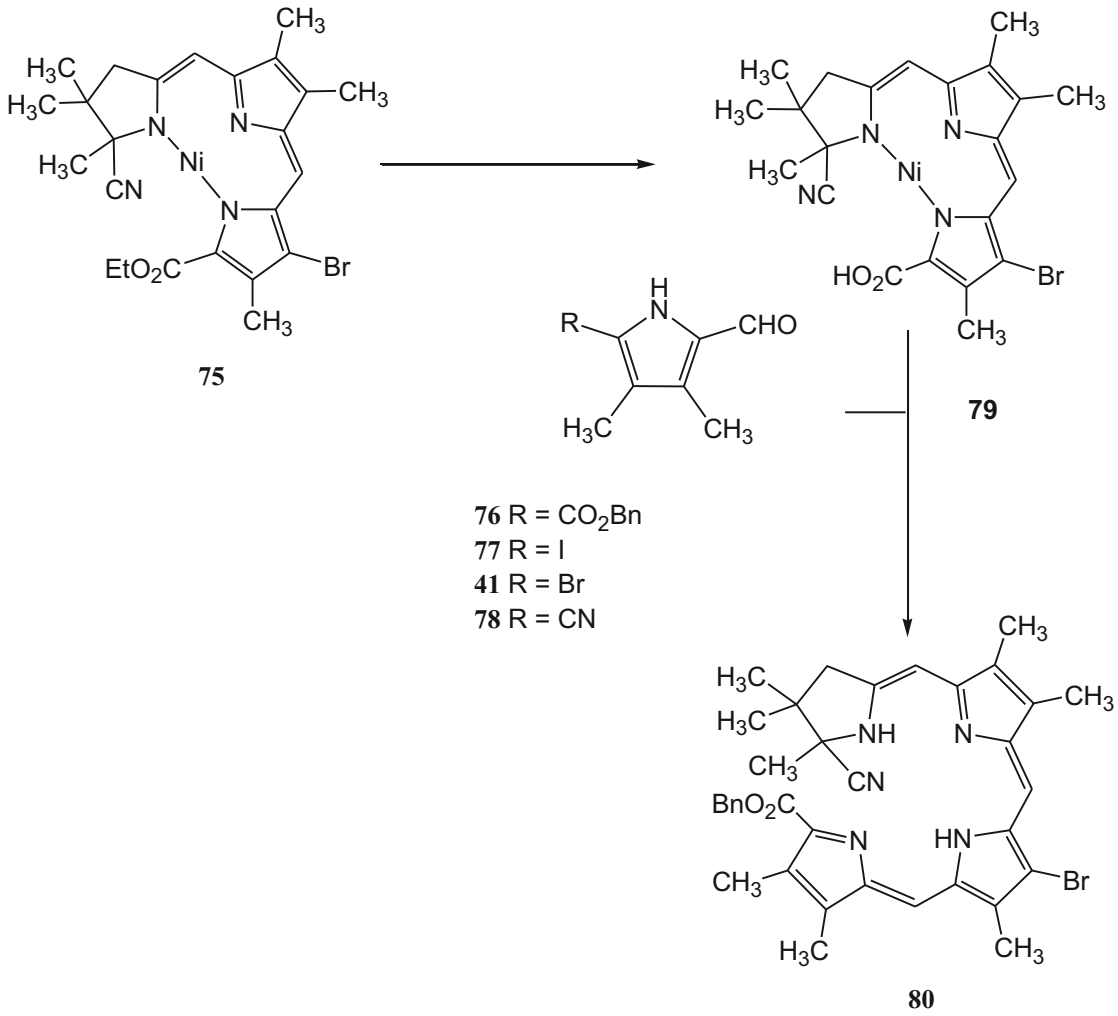
The formation of side product **72** could be supressed by using $P(C_6H_5)_3$ instead of $P(CH_2CH_2CN)_3$ in the sulfide contraction procedure. Complexation of these compounds with nickel(II) yielded two nickel complexes **74** and **75** (Scheme 28).



Scheme 28: Synthesis of the nickel complexes **74**, **75**

a:NBS, CH_2Cl_2, rt., 20 min.; **b**: DBU, CH_3CN, rt., 40 min.; **c**: 1) TFA, $P(Ph)_3$, benzene, reflux, 20 min.; **d**: $Ni(OAc)_2.4\ H_2O$, NaOAc, MeOH/CH_2Cl_2, rt., 20 min., (35.7 %).

3.5.3 Studies directed to synthesis of bilin 80



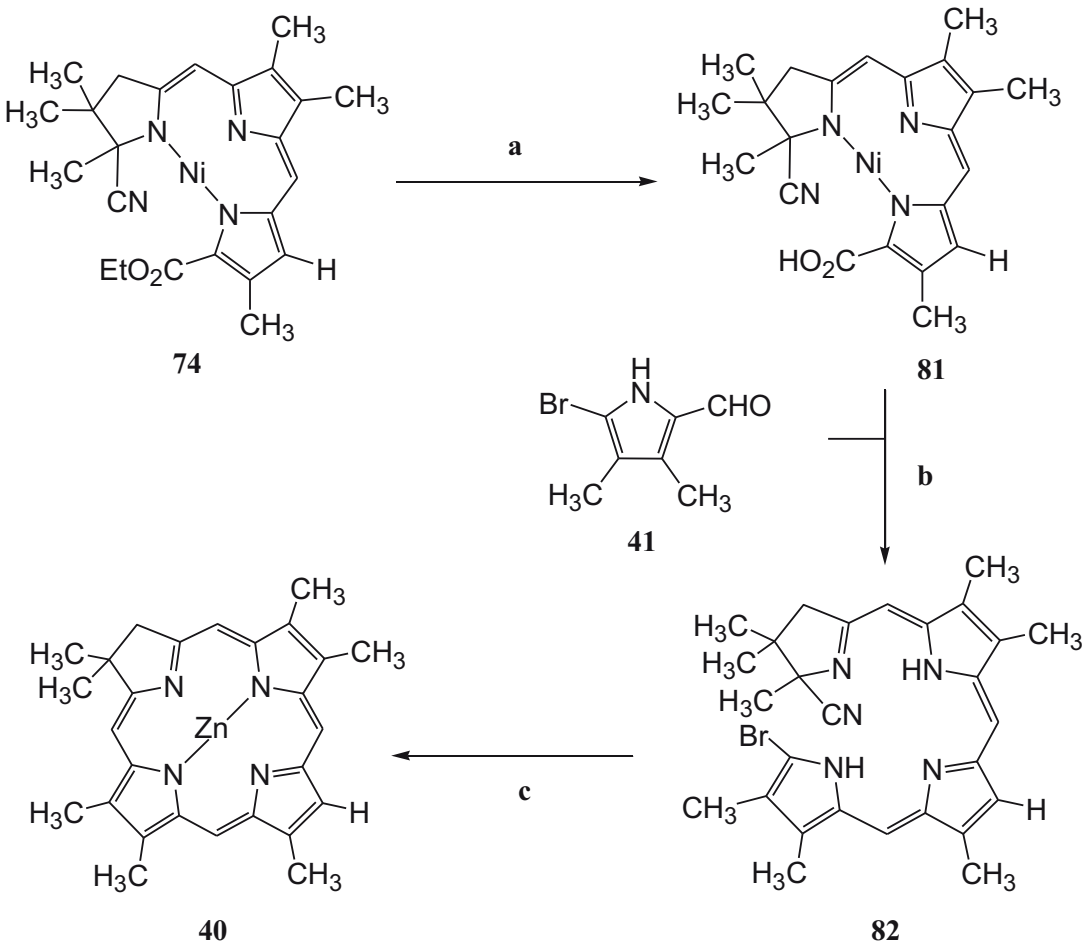
Scheme 29: Synthesis of bilin **80**

a: KOH, MeOH/H_2O, THF, 70 °C, 30 min.; **b**: **41** or **76-78**, $CHCl_3$, *p*-TsOH, reflux, 30 min.

According the synthetic procedure described in the Scheme 29, the ester group was cleaved to yield a polar deep violet compound. With this intermediate assumed as carboxylic acid **79** of tricyclic nickel complex **75**, the condensation reaction with different ring D building blocks (**41**, **76-78**) were performed. In all cases, decompositions were observed so that the preparation of bilin **80** failed.

3.5.4 Synthesis of a 12-unsubstituted chlorin

The nickel complex **74** produced as the side product (see Scheme 27) was used to synthesize 12-unsubstituted chlorin **40** (Scheme 30). This synthesis was carried out successfully following the general chlorin synthetic concept (see 2.2).



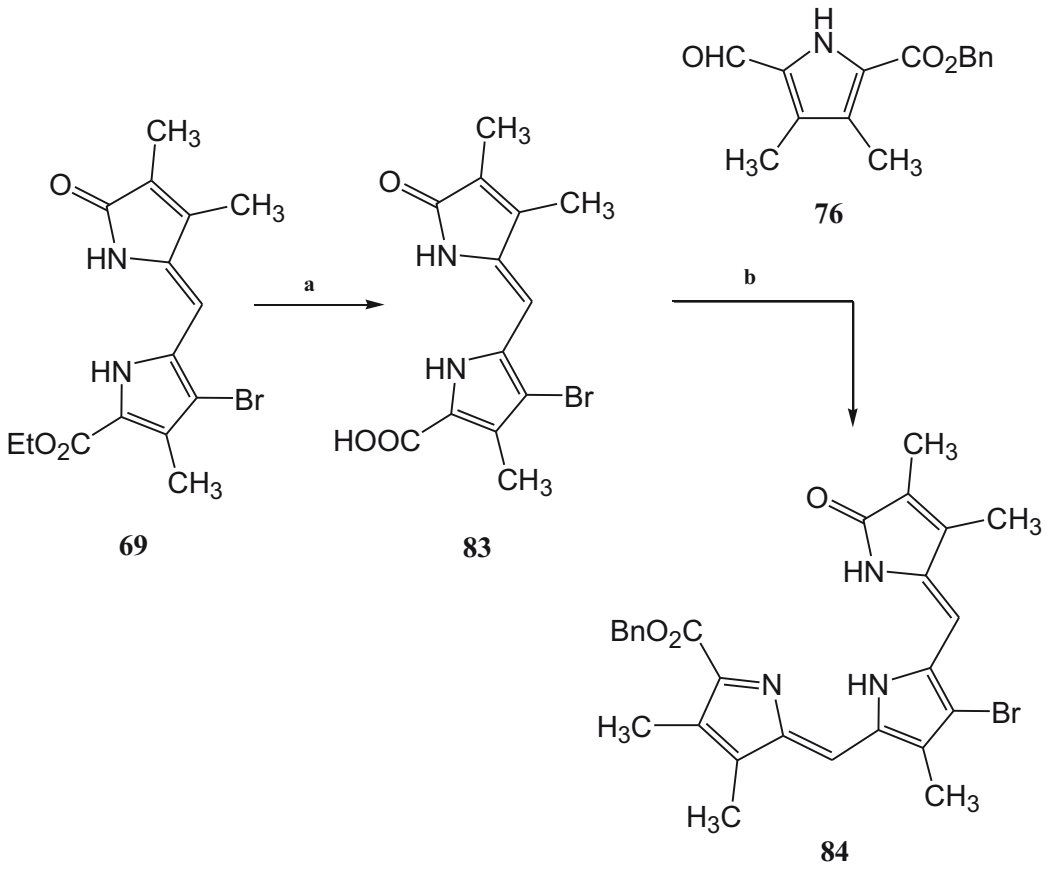
Scheme 30: Synthesis of 12-unsubstituted chlorin **40**

a: KOH, MeOH/H_2O, THF, 70 °C, 30 min; **b**: **41**, $CHCl_3$, p-TsOH, rt., 16 h, 62 %,

c: $Zn(CH_3COO)_2$, DBU, sulfolane*, 80 ^oC, 49.2 %.

3.5.5 Synthesis of a bromo-oxo-tripyrrin [77-79]

For formation of tricyclic lactam **84,** the ester function of the bicyclic lactam **69** was hydrolized followed by acid inducted condensation with pyrrole aldehyde **76**. The tripyrrin **84** was formed in 19 % yield (Scheme 31).

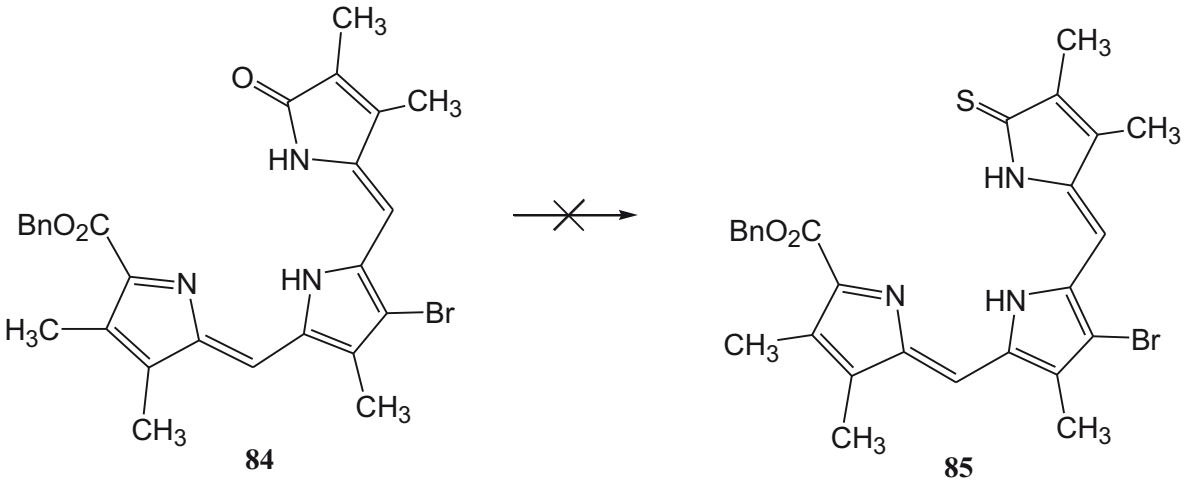


Scheme 31: Synthesis of oxo-tripyrrin **84**

a: THF, KOH, MeOH/H_2O (9+1), reflux, 1 h; **b**: TFA, $CHCl_3$, reflux, 2 h, 19 %.

3.5.6 Attempts to prepare a bromo-thiotripyrrin

Attempts to transform the tricyclic lactam **84** into its thio analogue using Lawesson's Reagent showed only decomposition. The observation is in agreement with previous studies which demonstrated that thiolactams are not accessible.[73]



Scheme 32: Attempts to form thiotripyrrin from tricyclic lactam **84**

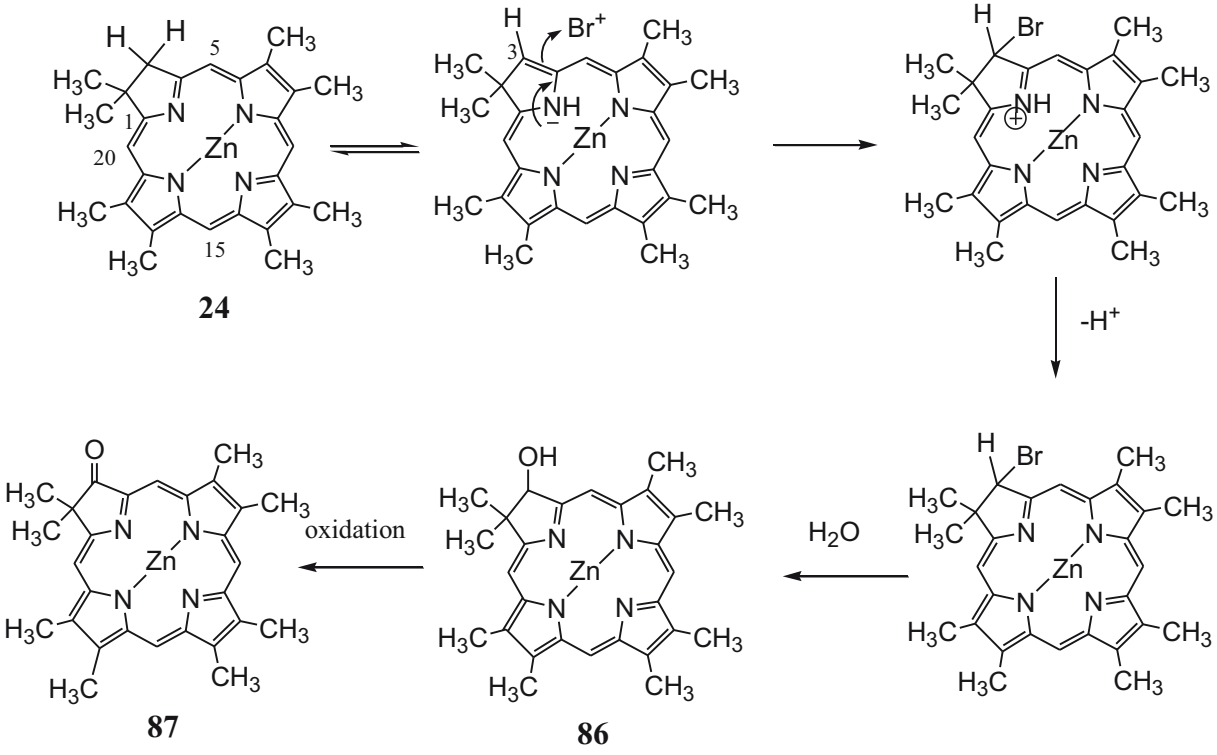
P_4S_{10} or Lawesson's Reagent, THF*, rt.

3.5.7 Studies directed to bromination of a geminally dimethylated chlorin

To investigate the bromination of chlorins, the standard reaction was performed based on the bromination of the geminally dimethylated chlorin **24**.

Previous studies[81-83] demonstrated that the electrophilic bromination of *β*-unsubstituted chlorins undergo selectively at the C-5 and C-20 positions. However, the bromination of chlorin **24** gave a mixture of hydroxyl substituted chlorin **86** and oxochlorin **87** unexpectly (Scheme 33).

The mechanism exhibited the tautomerization of ring A resulting the double bond between the position C-3 and C-4, as well as the enrichment of electron density at the C-4. The electrophylic brominated substitution at C-3 generated the substituted bromochlorin, which was easily hydrolized to form the hydroxylchlorin **86**. The oxidation of hydroxyl group gave the oxochlorin **87** as the second product.

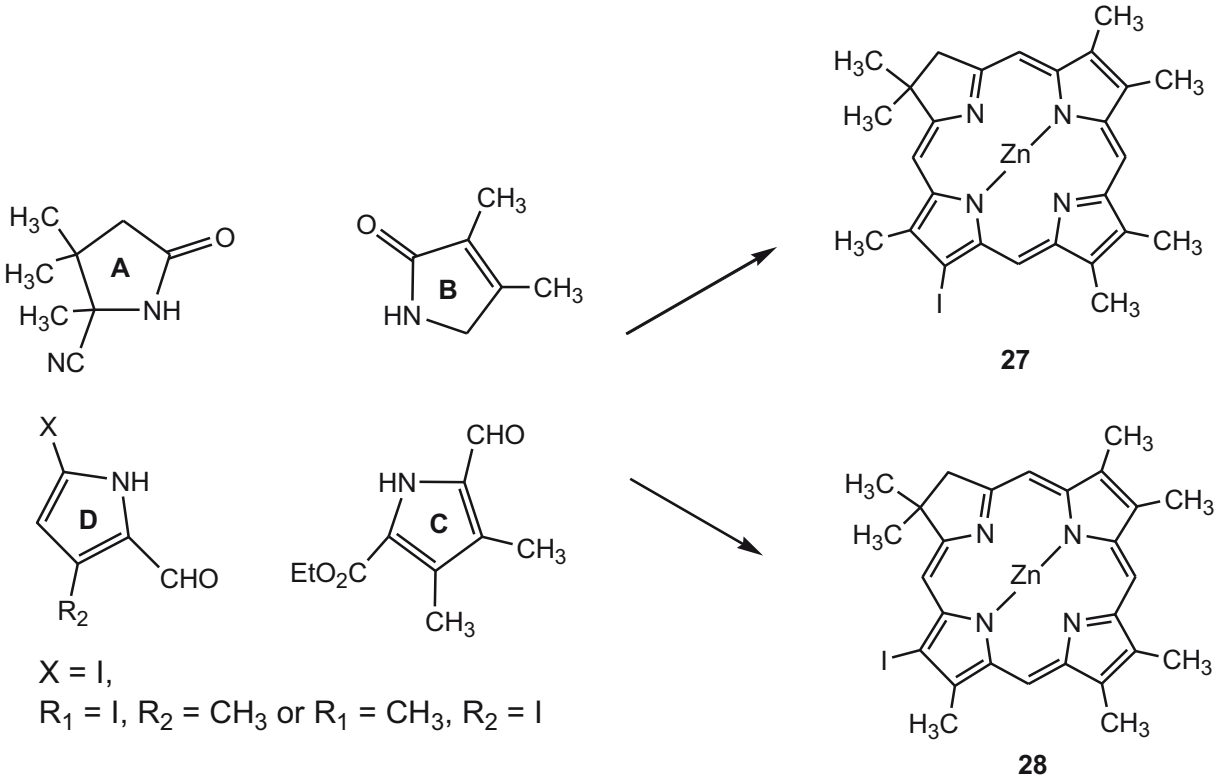


Scheme 33: Bromination of a geminally dimethylated chlorin **24** yielding hydroxylchlorin **86** and oxochlorin **87**

NBS, THF, -78 °C, 1 h, rt., 1h, 57.8 %

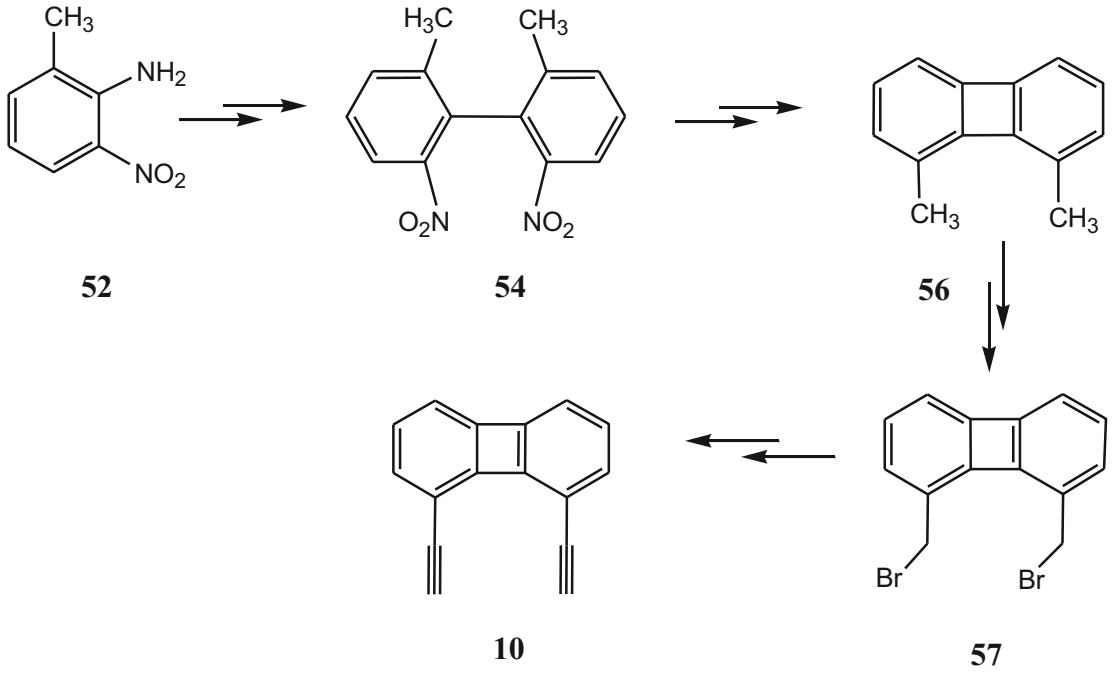
4. SUMMARY AND OUTLOOK

Based on the rings A, B, C and iodine substituted rings D, the total synthesis of 17-, 18-iodinated chlorins were achieved according to concept developed in our laboratory (Scheme 34).



Scheme 34: Total synthesis of 17-, 18-iodochlorins **27** and **28** from building blocks A-D

The synthesis of diethynylbiphenylene **10** as the spacer for connecting two chlorins 27, 28 was improved and modified along a route previously described in the literature.



Scheme 35: Synthesis of diethynylbiphenylene **10** as the spacer unit of of chlorin dyads

The subsequent connections of the 17-, 18- iodochlorins **27**, **28** and the spacer unit **10** were performed by the Shonogashira coupling. However, the yield of this reaction was not optimal due to the formation of side products. The final cofacial chlorin dyad **64** was characterized by HR-MS. The absorbance and fluorescence spectrum indicated the existance of the chlorin dyad in two conformations. This is in agrrement with the Semi-empirical PM3 calculations, in which the two chlorins are completely overlapping (eclipsed) **II** and partial overlapping (partial eclipsed) **I**. Both conformations represent arrangments which can be found in different photosynthetic systems.

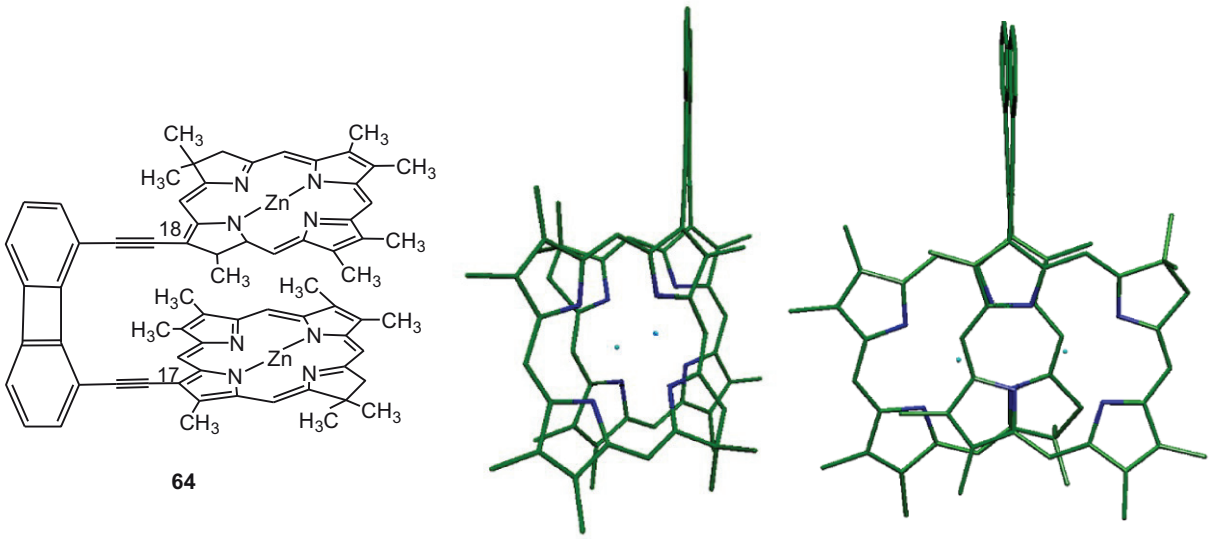
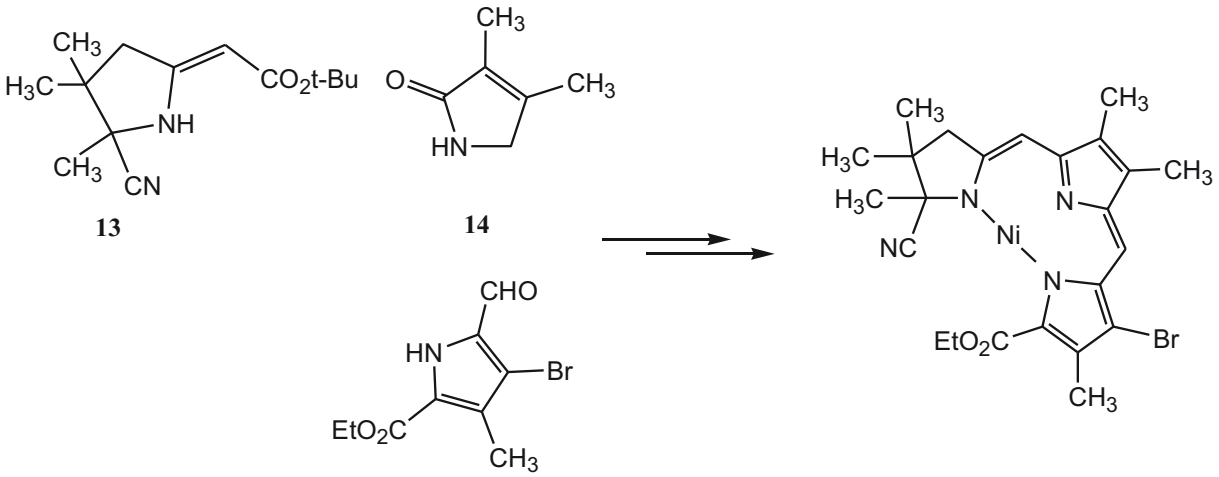


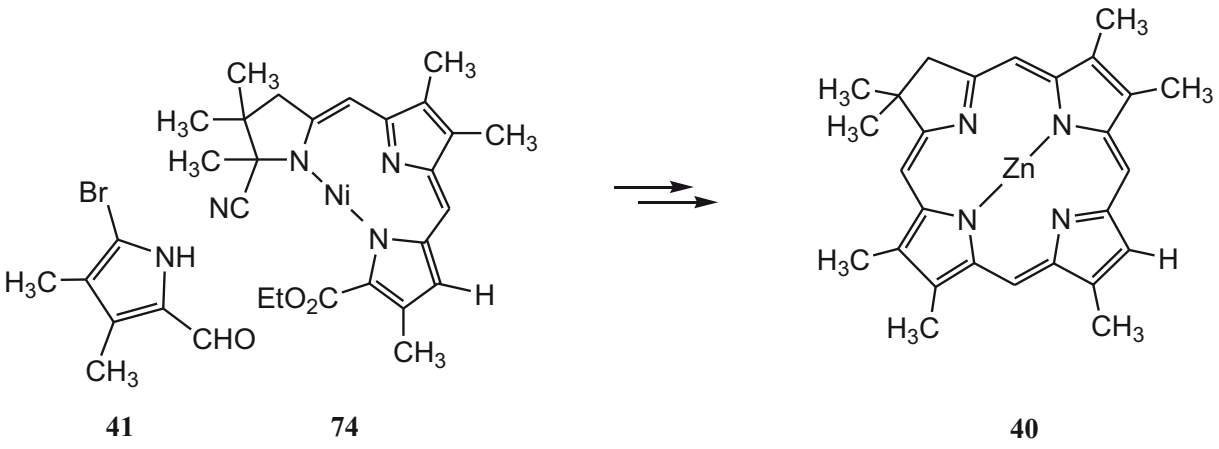
Figure 21: Chlorin dyad in two conformations

The investigation of 12-bromochlorin synthesis is based on the synthetic concept also applied for 17 and 18-iodochlorin. The bromo substituted pyrrole was employed as the corresponding ring C building block. The tricyclic nickel complex was formed as an intermediate with reasonable yields.



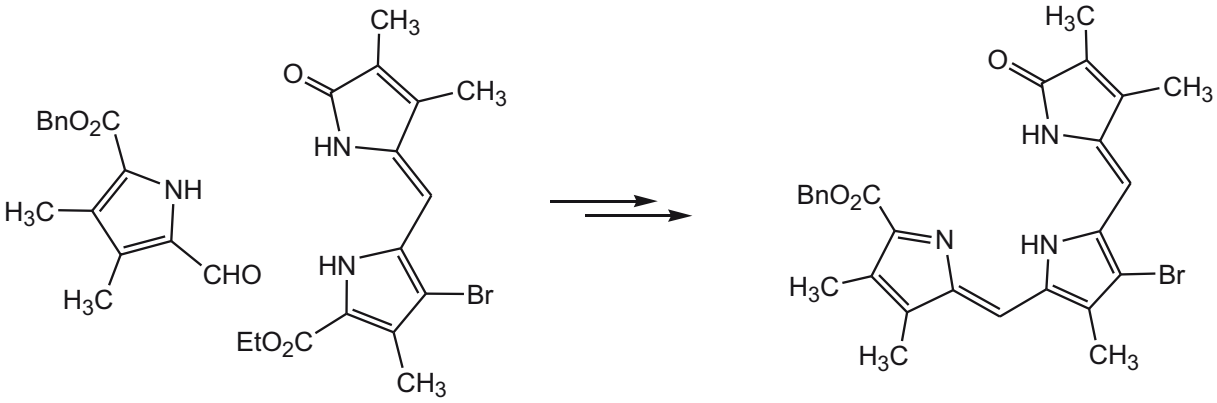
However the desired chlorin as the final product was not achieved due to decomposition of the bilin intermediate in the course of condensation of ring D building blocks to the tricyclic nickel complex.

An alternative concept for synthesis of 12-bromochlorin was approved by direct bromo substitution on the 12-unsubstituted chlorin **40**. This starting material was yielded based on the coresponding nickel complex **74**, a side product formed in the bromo nickel complex **75** synthesis process.



The directed bromination of chlorin was tested on the geminally dimethylated chlorin. However this starting material was easily accesible the bromonation yielding an undesired oxochlorin and hydxoxyl chlorin.

Another concept which should afford the 12-bromochlorin was investigated by attaching first the ring D buiding block **76** to the BC fragtment **69** to yield the oxo-tripyrrin **84**.



76 **69** **84**

However the thiolation of the oxo-tripyrrin showed completed decomposition of the formed product.

5. EXPERIMENTAL SECTION

5.1 GENERAL EXPERIMENTAL CONDITIONS

5.1.1 Quality of Chemicals and Solvents

The chemicals and reagents in the reaction were used without any purification. They were "synthesis" grade and purchased product of Fluka, VMR (Merck), Aldrich, Acros, Riedel-de-Häen, Lancaster and TCI.

All reactions and purification steps were performed with distilled solvents. For UV and fluorescence analysis, solvents were used in "HPLC" quality.

Solvents and reagents marked with (*) were dried and distilled under an argon atmosphere before usage according to literature procedures mentioned following:

Preparation of dry solvents and /or reagents (marked with * in next pages)

Acetonitrile	distilled over P_4O_{10}
Chloroform	distilled over P_4O_{10}
Benzene	distilled over sodium with indicator benzophenone
1,8-Diazabicyclo[5.4.0]undec-7-en (DBU)	distilled over molecular sieves
Dichloromethane	distilled over P_4O_{10}
Diethyl ether	distilled over sodium with indicator benzophenone
Ethanol	distilled over CaO
Methanol	distilled over CaO
Sulfolane	distilled over CaH_2
Tetrahydrofurane	distilled over sodium with indicator benzophenone
Toluene	distilled over sodium with indicator benzophenone
Triethylamine	distilled over CaH_2
Pyridine	distilled over molecular sieve

5.1.2 Analytical Instruments

Melting points (Mp)

The melting point determination was performed on a Reichert Thermovar hot stage and melting point apparatus from Gallenkamp Company. The results observed are uncorrected in both cases.

Infrared Spectroscopy (IR)

Spectra were recorded on a Paragon 500 FT-IR spectrometer from Perkin-Elmer with a resolution of 4.0 cm^{-1}. The relative band intensities were designated s (strong intensity), m (medium intensity), w (weak intensity) of band and br (broad band).

Ultraviolet and VIS Spectroscopy (UV/VIS)

UV/VIS measurements were performed on a Cary 50 spectrometer of Varian. Solutions with the concentration range 0.510^{-5} to $5*10^{-5}$ molar were used for the quantitative measurement. The absorption maxima at a wavelength λ were recorded as the molar extinction coefficient ε.

$$A = \log \frac{I_0}{I} = \varepsilon \ c \cdot d$$

A = absorbance at a wavelength λ

ε = molar extinction coefficient in cm 2 $mmol^{-1}$ or $mol^{-1}*dm^3*cm^{-1}$

c = concentration $mol.L^{-1}$

d = layer thickness in cm

Fluorescence Spectroscopy

The fluorescence determinations were performed on a LS50B fluorescence spectrophotometer from Perkin-Elmer. The particular excited wavelength λ_{exc} and the emitted wavelength λ_{em} were given in nm. Samples were measured in a molar concentration range of about 10^{-6} ($molL^{-1}$).

Nuclear Magnetic Resonance Spectroscopy NMR (^{1}H and ^{13}C-NMR, and NOE experiments)

NMR spectra were recorded by a Bruker-Daltonik DPX-200 (υ: ^{1}H = 200 MHz, ^{13}C = 50 MHz), or AM-360 (υ: ^{1}H = 360 MHz, ^{13}C = 90 MHz) spectrometer with 0.5 mL deuteriated solvent in a NMR tube of 5 mm diameter at the room temperature. The standard was set up by

the spectrometer software from Bruker Daltonic. The "lock in" was carried out on the respective solvent signal. The chemical shift δ (in ppm) was determined using deuterated solvent residues. The fine structure of proton signals was described by chemical shifts (δ) in part per million (ppm) and the multicity were quoted by s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets) and m (multiplet), The coupling constants ^{x}J relate to ^{1}H, ^{1}H coupling constants, in which x represents the number of bonds between the coupled nuclei.

Mass Spectrometry (MS)

The MS measurements were recorded on the double focusing mass spectrometers MAT 8200 and MAT 95 and on an electrospray mass spectrometer from Bruker Esquire LC Daltronic. Samples were measured by direct inlet method. The electron-impact ionization (EI) was performed with an ionization energy of 70 eV at a temperature, of 200 °C, if not noted. The electrospray ionization (ESI) was performed with a given solvent and a sample addition of 2 mL/min using direct inlet.

The spectrum, which had the molecule peak group with the largest percentage, was used for analysis. Only the peaks with a relative intensity of more than 10% were determined for analysis. Critical peaks were not noted in the structural determination.

High-resolution Mass Spectrometry (HR-MS)

High resolution spectrums were obtained on a double-focusing mass spectrometer MAT 8200 from Finnigan MAT company using the peak-matching method and on an APEX Qe 9.4T (superconducting magnet) unit with Apollo II electrospray source and Qh unit (quadrupole Filters included).

The reference substance Perefluxuorkerosin (PPR) was used as the reference substance and the resolution R was stated.

5.1.3 Chromatography

Thin Layer Chromatography (TLC)

TLC was performed on aluminium plates coated with silica gel 60 F254 (20x20 cm) or with aluminum oxide ALOX/UV254 from Fluka. The layer thickness was 0.2 mm. Band detections were obtained using a fluorescent lamp at wavelengths of 254, 366 nm or in an

iodine chamber.

Flash Chromatography

Flash chromatography was carried out using silica gel 32-63 µm 60 Å from ICN Biomedicales or aluminum oxide (ALOXN II-III, neutral, activity II-III) of the company ICN Biomedicals. The columns were packed by the slurry method (by slurry and degassing) in the indicated eluent. The separation was performed with normal or slightly elevated pressure.

Column Chromatography

The chromatography was carried out on silica gel 32 - 63 µm 60 Å from ICN Biomedicales or aluminum oxide (ALOXN II-III, neutral, activity II-III) of the company ICN Biomedicals. Packing of the column was performed by the slurry method using the indicated solvent system.

5.1.4 Formulas and Abrreviations

The abbreviations are generally used according to CAS Standard Abbreviations & Acronyms. Other abbreviations used are mentioned below:

aq.	aqueous
BRN	Beilstein registration number
Bn	benzyl
Bp	boiling point
CAN	ammoniumcer (IV)nitrat [$(NH_4)_2Ce(NO_3)_6$]
CAS-No.	CAS registration number
EtOAc	ethyl acetate
ether	diethyl ether
et	ethyl
eq.	equivalent(s)
h	hour
lit.	literature
m	medium
Me	CH_3
min.	minute
Mp	melting point

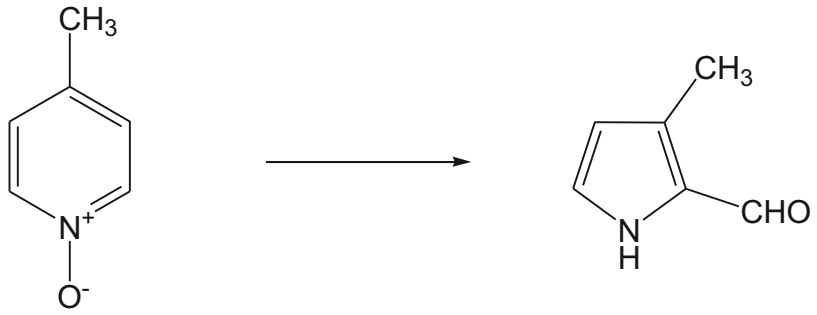
PE	petroleum ether
rel.	relative
rac.	racemic
rt.	room temperature
s.	strong
sat.	saturated
sol.	solution
THF	tetrahydrofurane
th.	theoretical
TEA	triethylamine
w	weak

5.1.5 References for CAS and BRN numbers

The respective numbers are stated at the end of the analytic data of a substance. If no number was noted, the substances were not referenced in the MDL Beilstein Crossfire Commander V6 (version 7.1) database at the time of the literature search.

5.2 SYNTHESIS OF DIFFERENT RING D BUILDING BLOCKS[52]

5.2.1 Synthesis of 3-methyl-1*H*- pyrrole-2-carbaldehyde (48)



47

C_6H_7NO

109.13

48

C_6H_7NO

109.13

The solution of 3.6 g (0.033 mmol) γ-piclolin-N-oxide and 120 g $CuSO_4.5H_2O$ (0.48 mol) in 600 mL water was irradiated by an irradiation apparatus with a high intensive mercury lamp (500 W). After 44 hours, the green-brown reaction mixture was extracted three times with 100 mL portions of diethylether. The combined organic layers were dried through a plug of cotton and the solvent was removed by rotary evaporator. The dark brown residue was purified by column chromatography (50 g of silica gel, dichloromethane/ethyl acetate 9:1) to give the formylpyrrol **48** (473 mg, 13 %) as colorless crystals.

Mp: 95 ^oC (CH_2Cl_2);

R_f: 0.5 (silica gel, CH_2Cl_2/EtOAc, 9:1);

IR (KBr): $\tilde{\nu}$ = 3244.9 (s, br., NH), 2856 (w, CH_3), 1629 (s, C=O), 1489 (m), 1430 (m), 1342 (m), 1175 (m), 1025 (m), 805 (s), 769 (s), 729 (m), 623 cm^{-1} (w);

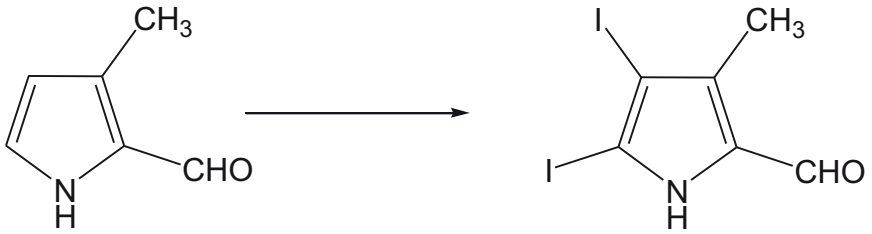
^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.4 (s, 3H, C**H**$_3$), 6.15 (s, 1H, 5-C**H**), 7.02 (s, 1H, 4-C**H**), 9.27 ppm (s, br., 1H, 1-N**H**), 9.65 (s, 1H, C**H**O);

MS (EI, 70 eV, 200 °C): *m/z* (% rel. intensity) = 109 (100) $[M]^+$, 108 (68) $[M-H]^+$, 80 (36) $[M-CHO]^+$, 53 [M-CHO-HCN]+, 40 (16);

BRN: 107876;

CAS-No: 24014-18-4.

5.2.2 Synthesis of 4,5–diiodo-3-methyl-1*H*- pyrrole-2-carbaldehyde (26)



48 **26**

C_6H_7NO $C_6H_5NOI_2$

109.13 360.92

To a solution of pyrrole **48** (50 mg, 0.48 mmol) in 5 mL of DMF* was added a solution of NaOH (65 mg, 1.6 mmol, 3.5 eq.) in 2mL water.A solution of iodide (350 mg, 1.4 mmol, 3 eq.) in 20 mL DMF* was then dropped slowly for 30 minutes. The reaction mixture was heated to 45 °C for 2 hours. After cooling, the solution of $Na_2S_2O_3$ (20 %) was dropped until the iodide color disappeared then the mixture was extracted 2 times with 20 mL portions of CH_2Cl_2. After removing the solvent, the organic residue was purified by column chromatography (silica gel, CH_2Cl_2/EtOAc, 9:1) and recrystallized from THF/n-hexan to afford pyrrole **26** (65.3 mg, 39.5 %) as colorless crystals.

Mp: 215 °C (THF/n-hexane);

R_f: 0.6 (silica gel, CH_2Cl_2/EtOAc, 9:1);

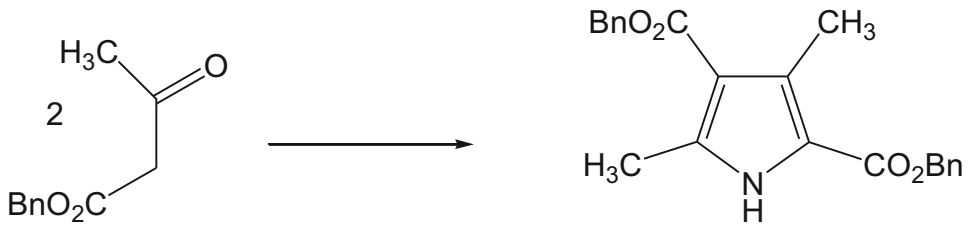
IR (KBr): $\tilde{\nu}$ = 3435 (s, br., NH), 3229 (s, N-H), 2851 (w, CH_3), 1627 (s, C=O), 1635 (s), 1407 (m), 1354 (s), 1206 (m), 1022 (m), 1005 (m), 827 (m,), 729 (m), 495 cm^{-1} (w);

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.32 (s, 3H, C**H**$_3$), 9.42 (s, br.,1H, N**H**), 9.63 ppm (s,1H, C**H**O);

MS (EI, 70 eV, 200 °C): *m/z* (% rel. intensity) = 452 (100) $[M]^+$, (9) $[M\text{-}CHO]^+$, 233 (5) $[M\text{-}I]^+$, 205 (4) $[M\text{-}CHO\text{-}I]^+$, 179 (3), 107 (3), 79 (4), 51 (6).

HR-MS [EI, $C_6H_5ONI_2$, R ≈ 10000]: Calculated: 360.84607;
Measured: 360.84713.

5.2.3 Synthesis of benzyl 3,5-dimethyl-1*H*-pyrrole-2,4-carboxylate (44)



43 **44**

$C_{11}H_{12}O_3$ $C_{22}H_{21}NO_4$

192.20 363.42

Benzyl acetoacetate (40 mL, 0.23 mol) (d = 1.114 g/mL) was dissolved in 50 mL of acetic acid and the solution was cooled to about 0 °C. The solution of $NaNO_2$ (10 g, 0.144 mol, 1.3 eq.) in 20 mL of water was dropped for 30 min.. The cooling mixture was stirred for further 4 hours. Zinc powder was further added while the temperature of the reaction mixture was kept at about 70 °C. The adding process was continuous until the temperature not increased. After the addition, the reaction was refluxed for 1 hour and poured into 700 g of crushed ice. The precipitate was separated from a filter funnel, washed with water and crystallized from benzene/PE to yield pyrrole **44 (**34.5 g, 79.6 %) as white crystals.

Mp: 135 °C (benzene/PE);

R_f: 0.6 (silica gel, CH_2Cl_2/EtOAc, 9:1);

IR (KBr): $\tilde{\nu}$ = 3309 (s, N-H), 3060, 3032 (w, =CH), 2963 (w, CH_3), 1699, 1664 (s, br, C=O), 1586 (w), 1567 (w), 1511 (w), 1489 (w), 1451 (m), 1432 (m), 1379 (w), 1342 (w), 1275 (s), 1260 (s), 1195 (s), 1111 (w), 1087 (s), 1047 (w), 1029 (w), 980 (w), 940 (w), 883 cm^{-1}(w);

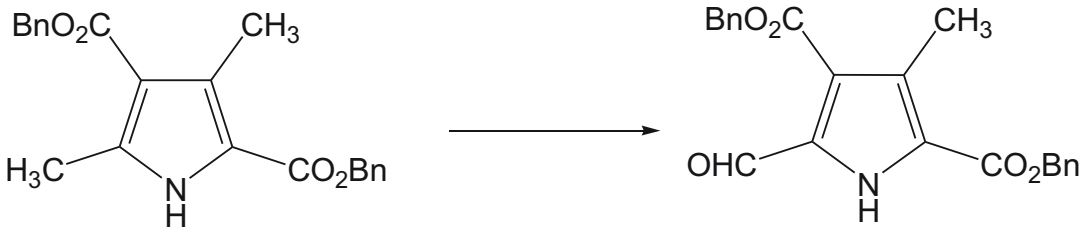
^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.50 (s, 3H, 5-C**H**$_3$), 2.59 (s, 3H, 3-C**H**$_3$), 5.30, 5.32 (s, s, 4H, 2 C**H**$_2$), 7.41 (m, aromatic, 10 H), 8.9 ppm (s, br, 1H, N**H**);

MS (EI, 70 eV 200°C): *m/z* (% rel. intensity) = 363 (13) $[M]^+$, 272(10) $[M-C_6H_5CH_2]^+$, 91 (100) $[C_6H_5CH_2]^+$, 65 (15) $[C_5H_5]^+$, 43 (28) $[C_4H_3]^+$;

BRN: 319664;

CAS-No: 52459-55-9.

5.2.4 Synthesis of benzyl 3-dimethyl-5-formyl-1*H*-pyrrole-2,4-dicarboxylate (45)



44 **45**

$C_{22}H_{21}NO_4$ $C_{22}H_{19}NO_5$

363.42 377.13

To a solution of benzyl 3,5-dimethyl-1*H*-pyrrole-2,4-dicarboxylate **44** (2.2 g, 5.5 mmol) in 60 mL of THF* and 5 mL of acetic acid was dropped a solution of ammonium cerium(IV) nitrate $[(NH_4)_2Ce(NO_3)_6]$ (15.076 g, 27.5 mmol, 5 eq.) in 30 mL water for 1 hour. The reaction mixture was further stirred for one hour at rt.. To terminate the reaction, 300 mL of water was added, the mixture was then extracted three times with 50 mL portions of dichloromethane. The combined organic extracts were washed with 50 mL of sat. aq. $NaHCO_3$ solution. The organic phase was dried through a plug of cotton and the solvent was removed by rotary evaporator. The given residue was purified by column chromatography (50 g of silica gel, dichloromethane/EtOAc 19:1). The crude product was crystallized from $CHCl_3$/n-pentane to afford benzyl 5-formyl-3-methyl-1*H*-pyrrole-2,4-dicarboxylate **45** (1.35 g, 65 %) as colourless crystals.

Mp: 128 °C ($CHCl_3$/n-pentane);

R_f: 0.5 (silica gel, CH_2Cl_2/EtOAc, 19:1);

IR (KBr): $\tilde{\nu}$ = 3256 (s, br, N-H), 2902 (w, CH_3), 1708, 1694 (s, br, C=O), 1587(w), 1553 (m), 1483 (m), 1465 (m), 1455 (m), 1381 (w), 1362 (w), 1337 (w), 1257 (s, C-O-C), 1231 (m), 1194 (s), 1120 (m), 1084 (w), 1029 (w), 946 (w), 913 (w), 878 (w), 828 cm^{-1}(w);

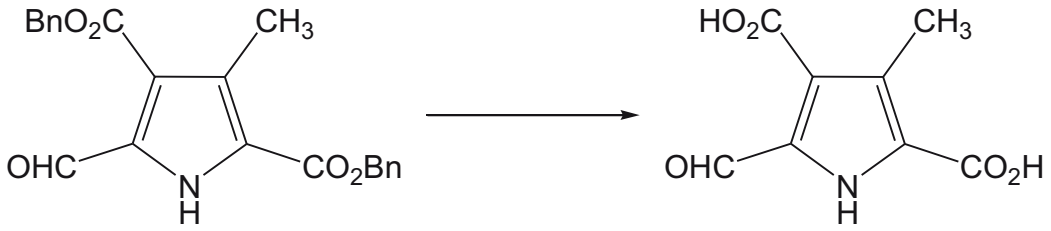
^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.62 (s, 3H, C**H**$_3$), 5.36, 5.38 (s, s, 4H, 2 C**H**$_2$), 7.41 (m, aromatic, 10 H), 9.63 (s, br, 1H, N**H**), 10.24 ppm (s, 1H, C**H**O);

MS (EI, 70 eV, 200 °C): *m/z* (% rel. intensity) = 377 (7) $[M]^+$, 359 (4) $[M\text{-}CO]^+$, 286 (24) $[M\text{-}C_6H_5CH_2]^+$, 271 (15) $[M\text{-}C_6H_5CH_2\text{-}CH_3]^+$, 180 (6) $[M\text{-}C_6H_5CH_2\text{-}CH_3\text{-}C_6H_5]^+$, 162 (6), 91 (100) $[C_6H_5CH_2]^+$, 65 (7) $[C_5H_5]^+$;

BRN: 498286;

CAS-No: 52649-13-5.

5.2.5 Synthesis of 3-dimethyl-5-formyl-1*H*-pyrrole-2,4-carboxylic acid (46)



45 **46**

$C_{22}H_{19}NO_5$ $C_8H_7NO_5$

377.13 197.15

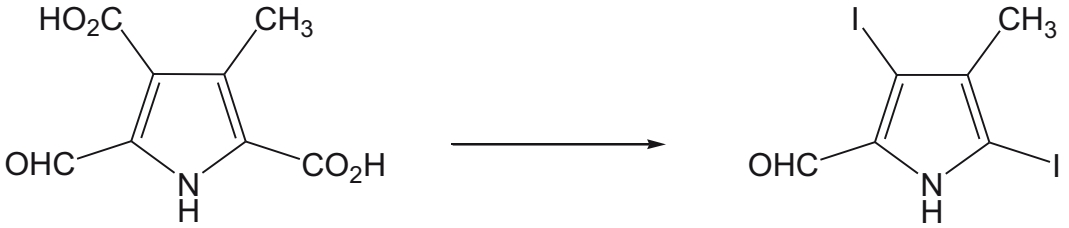
Benzyl 3-dimethyl-5-formyl-1*H*-pyrrole-2,4-dicarboxylate **45** (1.45 g, 3.84 mmol) was dissolved in 10 mL THF * and mixed with 2-3 drops of triethylamine*. The flask was evacuated and gassed with argon. This process was repeated 2 times and the reaction mixture was added with 150 mg Pd-carbon catalyst. The flask was again evacuated 2 times, gassed

with hydrogen and the reaction mixture was stirred at rt. and controlled by TLC. At the end of the reaction, the mixture was filtered through celite and washed with 50 mL of methanol. The solvent was then removed by rotary evaporator to give 3-dimethyl-5-formyl-1*H*-pyrrole-2,4-carboxylic acid **46** (757 mg, 3.83 mmol, quantitative) as the colourless powder, which was further implied without any characterization.

BRN: 170129;

CAS-No: 79754-38-4.

5.2.6 Synthesis of 2,4-diiodo-3-methyl-1*H*-pyrrole-2-carbaldehyde (25)



46 **25**

$C_8H_7NO_5$ $C_6H_5NOI_2$

197.15 360.92

A three-neck flask with a dropping funnel and a thermometer was charged with a solution of dicarboxylic acid **46 (**210 mg, 1.06 mmol) and $NaHCO_3$ 358 g (4.24 mmol, 4 eq.) of in 10 mL water then the mixture was heated to 70 ^oC. A solution of iodide (430 mg, 2.12 mmol, 2eq.) and potassium iodide (1.05 g, 6.36 mmol, 6 eq.) in 15 mL of water was dropped for 30 min.. The reaction mixture was stirred for further 20 min. at 70 ^oC. After cooling, the mixture was added with some drops of sat. $Na_2S_2O_3$ solution to neutralize the excess of iodine. The resulting mixtre was filtered through a pad of celite and the aq. filtrate was then extracted 3 times with 30 mL portions of CH_2Cl_2. The combined organic phases were washed with 30 mL of sat. aq. NaCl solution and dried through a plug of cotton. The solvent was removed by rotary evaporator to give the crude product, which was purified by column chromatography (20 g silica gel, dichlomethane/ethylacetate 9:1) and recrystalized from $CHCl_3$/n-pentane to obtain diiodopyrrole **25** (96.1 mg, 25 %) as colourless crystals.

Mp: 175 °C ($CHCl_3$/n-pentane);

R_f: 0.5 (silica gel, CH_2Cl_2/EtOAc, 9:1);

IR (KBr): $\tilde{\nu}$ = 3182.1 (s, br, N-H), 2839 (w, CH_3), 1708, 1640 (s, br, C=O), 1430 (m), 1382 (m), 1330 (m), 1381 (w), 1227 (m), 1030 (w), 793 (m), 757 (w), 495 (w, C-I) cm^{-1}(w);

^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.10 (s, 3H, C**H**$_3$), 9.19 (s, 1H, C**H**O), 9.21 ppm (s, br, 1H, N**H**);

MS (EI, 70 eV, 200 °C): *m/z* (% rel. intensity) = 361 (100) $[M]^+$, 332 (4) $[M\text{-}CHO]^+$, 233 (8) $[M\text{-}I]^+$, 107 (7) $[M\text{-}I\text{-}I]^+$, 79 (12), 51 (18), 28 (9);

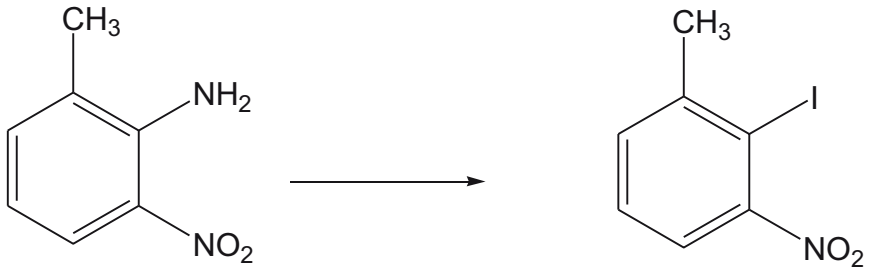
BRN: 1526401;

CAS-No: 49569-09-7.

5.3 SYNTHESIS OF A DIETHYNYLBIPHENYLENE SPACER

[58, 64,65]

5.3.1 Synthesis of 2-iodo-3-methylnitrobenzene (53)



52

$C_7H_8O_2N_2$

152.15

53

$C_7H_6O_2NI$

263.04

A three-necked flask with a dropping funnel, an internal thermometer and a big stirrer was charged with 2-methyl-6-nitro aniline **52** (25 g, 164.5 mmol). This starting material was then suspended in 125 mL of concentrated hydrochloric acid and the mixture was cooled to 0 °C. A solution of sodium nitrite (14.25 g, 206.5 mmol, 1.2 eq.) in 50 mL of water was added dropwise slowly so that the temperature was not higher than 10 °C. After the addition, the reaction solution was stirred for further 30 min.. The mixture was then poured to a solution of potassium iodide (54.5 g, 328.27 mmol, 2 eq.) in 210 mL water cooled to 0 °C and stirred for further 10 min.. To remove the excess of iodide, 10 mL portions of sat. $Na_2S_2O_3$ solution was added to the reaction mixture until the dark colour disappeared. The precipitate was filtered through a filter funnel and washed with 500 mL of water. The crude product was recrystalized from ethanol to give 2-iodo-3-methyl nitrobenzene **53** (39.11 g, 90.4 %) as pale yellow powder.

Mp: 61 ^{o}C (ethanol);

R_f: 0.7 (silica gel, PE/CH_2Cl_2 1:1);

IR (KBr): $\tilde{\nu}$ = 3073 (w, C-H, aromatic), 2946 (w, CH_3), 1530 (s, NO_2), 1450 (m), 1430 (w), 1370 (s, NO_2), 1270 (w), 1186 (w), 1023 (s, C-I), 910 (m), 806 (s, C-H aromatic), 786 (s, C-H aromatic), 730 (m), 693 (m), 530 cm^{-1}(w);

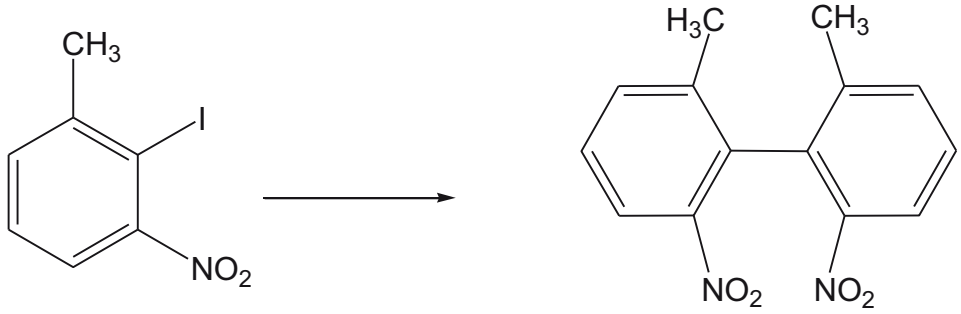
^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.6 (s, 3H, C**H**$_3$), 7.3-7.5 ppm (m, 3H, 3 C**H**-benzene);

MS (EI, 70 eV, 200 °C): *m/z* (% rel. intensity) = 263 (100) $[M]^+$, 217 (15) $[M-NO_2]^+$, 136 (6) $[M-I]^+$, 90 (70) $[M-I-NO_2]^+$, 78 (8), 63 (16);

BRN: 2691415;

CAS-No: 6277-17-4.

5.3.2 Synthesis of 6,6'-dimethyl-2,2'-dinitrobiphenyl (54)



53 **54**

$C_7H_6O_2NI$ $C_{14}H_{12}N_2O_4$

263.04 272.26

A 500 mL round flask was charged with 2-iodo-3-methylnitrobenzene **53** (25.5 g, 0.093 mol) in 100 mL of DMF* and copper powder (17.85 g, 0.278 mol, 3 eq.). The mixture was charged with argon and heated to 160 °C for 4 hours under argon atmosphere. After cooling, additional copper (17.85 g, 0.278 mol, 3 eq.) was added and the mixture was heated again to 160 °C for 2 hours. To remove the solid, the mixture was filtered through a pad of of celite then the inorganic residue was washed with 50 mL portions of diethylether. The combined organic solution was concentrated under reduced pressure and the residue was poured to 800 mL of water. The mixture was kept in the fridge overnight to afford the crude solid product,

which was recrystallized from ethanol to yield dinitrobiphenyl **54** (8.12 g, 61.6 %) as light yellow crystals.

Mp: 109 °C (ethanol);

R_f: 0.5 (silica gel, PE/CH_2Cl_2 1:1);

IR (KBr): $\tilde{\nu}$ = 3093 (w, C-H, aromatic), 2913, 2853 (w, CH_3)1603 (w, C=C, aromatic), 1530(s, NO_2), 1456 (m, aromatic), 1350 (s, NO_2), 1286 (m), 1156 (w), 1106 (w), 910 (w), 816, 793, 740 (s, C-H), 673 cm^{-1} (w);

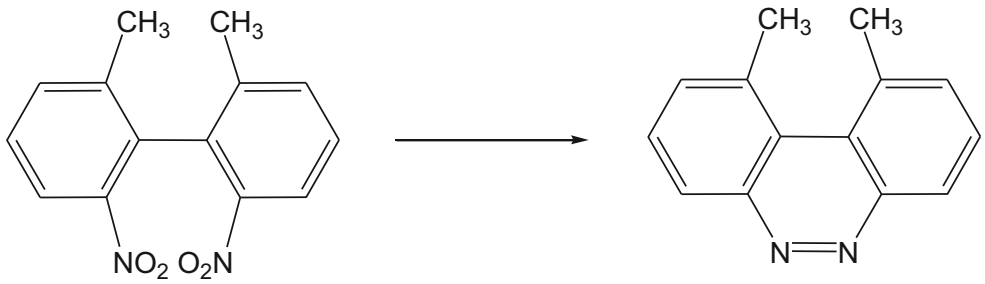
^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.0 (s, 6H, 2* 6–C**H**$_3$); 7.49 (dd, 2H, ^{3}J = 7.7 Hz, 8.10 Hz, 4,4'-C**H**), 7.93 (d, 2H, ^{3}J = 7.31 Hz, 5,5' –C**H**), 8.01 ppm (d, 2H, ^{3}J = 8.10 Hz, 3,3' –C**H**);

MS (EI, 70 eV, 200 °C): m/z (% relative intensity) = 272 (19) $[M]^+$, 255 (11), 226 (100) $[M-NO_2]^+$, 211 (3) $[M-NO_2-CH_3]^+$, 195 (10) $[M-C_2H_6NO_2]^+$, 178 (11), 165 (16), 152 (24), 139 (8), 115 (14), 77 (10);

BRN: 1996263;

CAS-No: 55153-02-1.

5.3.3 Synthesis of 1,10-dimethylbenzo[c]cinnoline (55)



54

$C_{14}H_{12}N_2O_4$

272.26

55

$C_{14}H_{12}N_2$

208.27

A two-necked round-bottomed flask equipped with magnetic stirrer, a dropping-funnel was charged with $LiAlH_4$ (5.34 g, 0.142 mmol) and 70 mL of diethyether*. The solution of 6,6'-dimethyl-2,2'-dinitrobiphenylene **54** (7.9 g, 0.029 mmol) in 70 mL benzene* was dropped slowly under argon so that the mixture was refluxed gently and turned to dark brown colour. After the addition was completed, the mixture was stirred for further 30 min., water was added dropwise carefully to neutralize the excess of $LiAlH_4$. The reaction mixture was filtered through pad of celite then washed with 30 mL portions of diethylether. The filtrate was concentrated under reduced pressure to give an orange oil, which was recrystallized from ethanol to form 1,10-dimethylbenzo[c]cinnoline **55** (3.74 g, 62 %) as orange crystals.

Mp: 114 ^{o}C (ethanol);

R_f: 0.5 (silica gel, CH_2Cl_2/EtOAc: 1:1)

IR (KBr): $\tilde{\nu}$ = 3054, 3005 (w, C-H aromatic), 2980, 2919 (w, CH_3), 1594 (w, N=N), 1568 (m, C=C), 1460 (m), 1430 (m), 1382 (s), 1337 (s), 1229 (m), 1169 (m), 1125 (m), 1095 (m) 968 (w), 910 (w), 793, 779 (s C-H aromatic), 704 cm^{-1} (m);

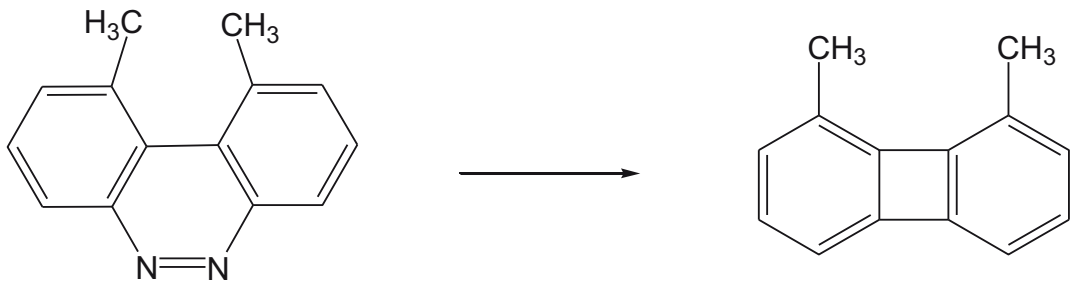
^{1}H-NMR (200 MHz, $CDCl_3$): δ = 2.65 (s, 6H, 2* –CH_3); 7.78 (m, 4H, Aryl-H); 8.59 ppm (m, 2H, Aryl-H);

MS (EI, 70eV, 200 ^{o}C): m/z (% relative intensity) = 208 (100) $[M]^+$, 180 (15) $[M\text{-}N_2]^+$, 179 (68) $[M\text{-}N_2\text{-}H]$, 178 (50) $[M\text{-}N_2\text{-}H_2]^+$, 165 (88) $[M\text{-}N_2\text{-}CH_3]$, 152 (11), 139 (5), 115 (4), 89 (12), 76 (9);

BRN: 159675;

CAS-No: 60984-22-7.

5.3.4 Synthesis of 1,8-dimethylbiphenylen (56)



55

$C_{14}H_{12}N_2$

208.27

56

$C_{14}H_{12}$

180.25

The transformation of 10-dimethylbenzo[c]cinnoline to 1,8-dimethylbiphenylen was performed by pyrolysis apparatus. For this purpose, a 10 mL round bottomed flask was charged with 1 g benzo[c]cinnoline **55** then connected to a quartz tube. This was surrounded by a pyrolysis furnace. A flask cooled with liquid nitrogen was connected to the other side of the tube. The apparatus was evacuated, the pyrolysis furnace was heated to 700 °C and the starting material was heated to 220 °C using a metal bath. From 160 ^{o}C, the benzo[c]cinnoline **55** was evaporated and partly condensed on the tube, which was evaporated by using the heating foam, leaving only a dark residue in the flask. The brown crude product was obtained on the other side of the tube. After an hour, the reaction was terminated and the apparatus was rinsed with CH_2Cl_2. The solvent was concentrated by vacuum and washed on the column of silica gel, eluted with (PE/CH_2Cl_2: 2:1) to give the yellow oil in the first fraction, which was further purified by column chromatography (silica gel, PE) to afford 1,8-dimethylbiphenylene **56** (240 mg, 27.9 %) as light yellow crystals.

Mp: 79 ^{o}C (ethanol);

R_f: 0.5 (silica gel, PE);

IR (KBr): $\tilde{\nu}$ = 3027 (w, C-H aromatic), 2915 (w, CH_3), 2846 (w, CH_3), 1663 (s, C=C), 1448 (m), 1388 (m), 1276 (w), 1227 (w), 1194 (w), 1151 (w), 1107 (w), 1034 (w), 883 (w), 810 (w), 754 (s, C-H, aromatic), 698 (s, C-H, aromatic), 625 (w), 457 cm^{-1} (w);

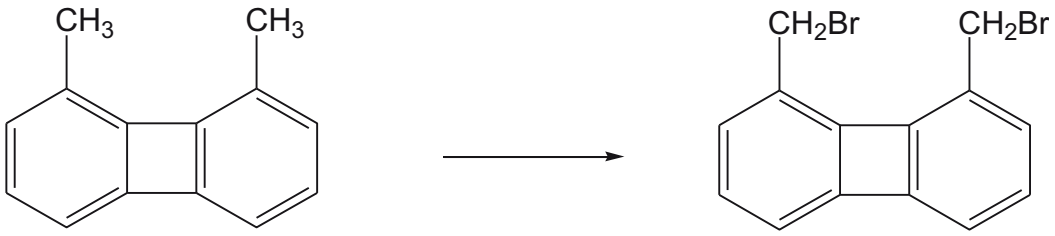
^{1}H-NMR (200 MHz, $CDCl_3$): δ = 5.45-6.7 (m, 6H, 6 C-**H** aromatic), 2.2 ppm (s, 6H, 2 C**H**$_3$);

MS (EI, 70 eV, 200 ^{o}C): m/z (% relative intensity) = 180 (100) $[M]^+$, 165 (28) $[M\text{-}CH_3]^+$, 152 (8), 139 (6), 90 (7), 76 (8);

BRN: 2042837;

CAS-No: 36230-17-8.

5.3.5 Synthesis of 1,8-bis(bromomethyl)biphenylene (57)



56 $C_{14}H_{12}$ 180.25

57 $C_{14}H_{10}Br_2$ 338.04

To a solution of 1,8-dimethylbiphenylene **56** (350 mg, 1.94 mmol) and N-bromosuccinimide (690 mg, 3.88 mmol) in 3 mL of CCl_4* was added 2 mg of dibenzoyl peroxide. The mixture was refluxed for 6 hours under light irradiation (150 W lamp). The hot mixture was filtered through paper filter and the residue was washed twice with hot CCl_4. The solvent was removed to give the solid mixture containing the staring material, mono(bromomethyl)biphenylen and the product, which was purified by column chromatography (50 g silica gel, cyclohexane). The crude product was then recrystallized from $CHCl_3$/n-heptane to yield 1,8-bis(bromometyl)biphenylene **57** (234 mg, 35 %) as a yellow solid.

Mp: 204 ^{o}C ($CHCl_3$/n-heptane);

R_f: 0.3 (silica gel, PE);

IR (KBr): $\tilde{\nu}$ = 3016 (w, C-H, aromatic), 1634 (m, aromatic), 1444 (m, aromatic), 1394 (m, aromatic), 1285 (w), 1245 (w), 1217 (w), 1188 (s), 1136 (w), 1095 (w), 1043 (w), 977 (w), 940 (w), 778 (s), 715 (s), 625 (s), 609 cm^{-1} (s);

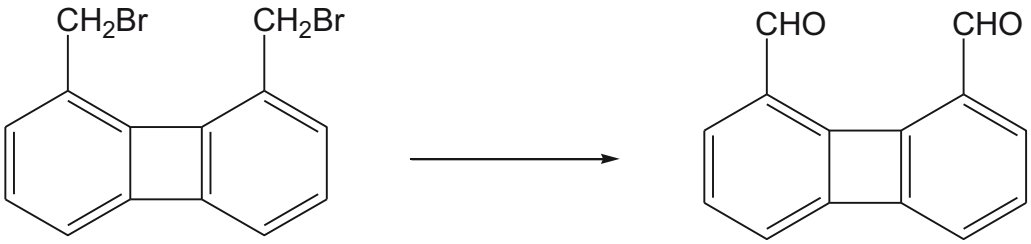
^{1}H-NMR (200 MHz, $CDCl_3$): δ = 6.55-6.88 (m, 6H, 6 C-H aromatic), 4.45 ppm (s, 4H, 2 CH_2Br);

MS (EI, 70eV, 220 ^oC): m/z (% relative intensity) = 340 (24) $[C_{14}H_{10}{}^{81}Br_2]^+$, 338 (48) $_{14}H_{10}{}^{81}Br^{79}Br]^+$, 336 (24) $[C_{14}H_{10}{}^{79}Br_2]^+$, 259 (84) $[C_{14}H_{10}{}^{81}Br^{79}Br\text{-}^{79}Br]$, 257 (84) $C_{14}H_{10}{}^{81}Br^{79}Br\text{-}^{81}Br]$, 178 (100) $[C_{14}H_{10}{}^{81}Br^{79}Br\text{-}^{79}Br]$, 152 (20), 88 (32), 76 (28);

BRN: 1970019;

CAS-No: 36396-04-0.

5.3.6 Synthesis of 1,8-diformylbiphenylene (58)



57 **58**

$C_{14}H_{10}Br_2$ $C_{14}H_8O_2$

338.04 208.22

A solution of 1,8-bis(bromomethyl)biphenylene **57** (200 mg, 0.591 mmol) and bis(tetrabutylammonium) dichromate (1.60 g, 2.18 mmol, 3.7 eq.) in 30 mL $CHCl_3$ was refluxed for 3 hours under argon atmosphere. After cooling, the reaction mixture was filtered through a pad of celite and washed with 30 mL portions of diethylether until no more product eluted. The combined solvent was removed by rotary evaporator and the crude product was purified by column chromatography (50 g silica gel, CH_2Cl_2/PE 1:1) and recrystallized from CH_2Cl_2 to yield 1,8-diformylbiphenylene **58** (96 mg, 78 %) as yellow crystals.

Mp: 124 °C (CH_2Cl_2);

R_f: 0.6 (silica gel, CH_2Cl_2);

IR (KBr) $\tilde{\nu}$ = 3112 (w, C-H, aromatic), 1698 (s, C=O), 1674 (s, C=O), 1657 (m, aromatic), 1381 (m), 1279 (w), 1251 (m), 1194 (w), 1127 (w), 973 (w), 945 (m), 778 (w), 765 (s), 739 (w), 700 cm^{-1} (w);

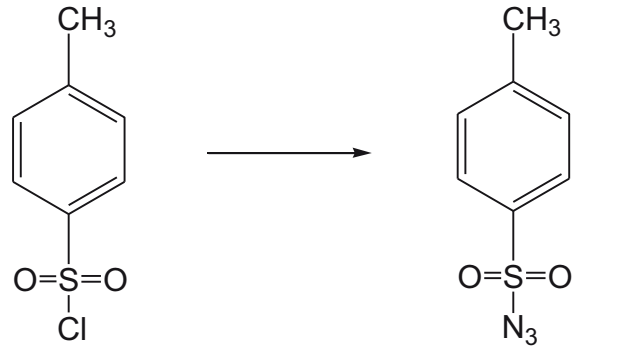
^{1}H-NMR: (200 MHz, $CDCl_3$): δ = 6.87 (d, ^{3}J = 7.5 Hz, 2H, 4,5-C**H**), 7.04 (dd, ^{3}J = 6.8 Hz, ^{3}J = 8.2 Hz, 2H, 3,6-C**H**), 7.29 (d, ^{3}J = 8.5 Hz, 2H, 2,7-C**H**), 10.33 ppm (s, 2H, C**H**O);

MS (EI, 70 eV, 200 °C): m/z (% relative intensity) = 208 (100) $[M]^+$, 180 (62) $[M\text{-}CO]^+$, 151 (68) [M-2CO-H], 126 (5), 99 (6), 76 (15);

BRN: 1871182;

CAS-No: 58746-94-4.

5.3.7 Synthesis of *p*-toluene sulfonylazide (61)



90 **61**

$C_7H_7O_2SCl$ $C_7H_7O_2N_3S$

190.65 197.22

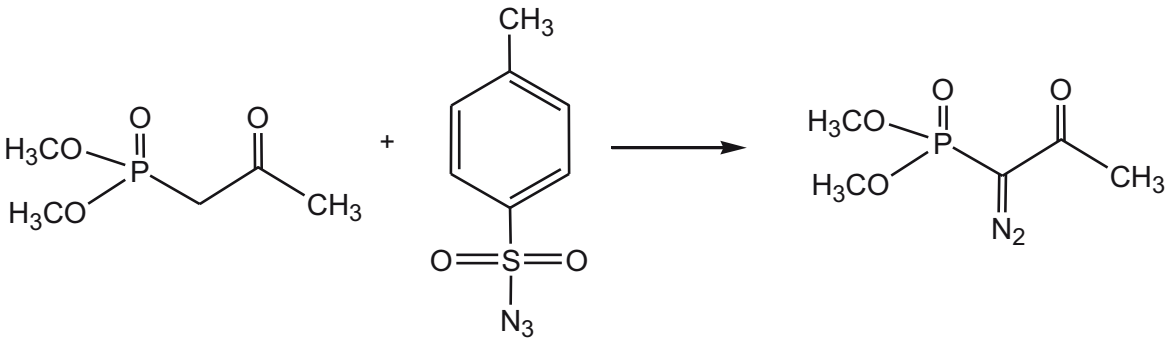
To a solution of *p*-toluenesulfonyl chloride **90** (2.86 g, 15 mmol) in 50 mL acetone/water (1:1) cooled to 0 °C was added sodium azide (1.07 g, 16.5 mmol, 1.1 eq.). The mixture was

stirred at 0 °C for 2 hours under argon atmosphere. After removing acetone by a rotary evaporator, the remaining aqueous mixture was extracted several times with 20 mL portions of diethyl ether. The organic phase was dried through a plug of cotton and concentrated by rotary evaporator to obtain quantitative yield of *p*-toluene sulfonylazide **61** as colourless oil. This compound was further implemented without further purification and characterization.

BRN: 4258947;

CAS-No: 941-55-9.

5.3.8 Synthesis of dimethyl-acetyl-diazomethylphosphonate (59)



60 **61** **59**

$C_7H_7O_2N_3S$ $C_5H_{11}O_4P$ $C_5H_9O_4P$

197.22 166.11 192.11

A two-necked round bottom flask equipped with a dropping funnel was charged with dimethyl-acetylphosphonate **60** (1.15 g, 6.9 mmol) and K_2CO_3 (1.36 g, 11.76 mmol, 1.7 eq.) in 10 mL of acetonitrile*. To this mixture a solution of *p*-toluene sulfonylazide **61** (2.32 g, 11.76 mmol, 1.7 eq.) in 10 mL acetonitrile* was added dropwise slowly. The end of the reaction was determined by TLC after about 1-2 hours. The reaction mixture was filtered through a pad of celite and washed exhaustively with diethyl ether. After removing the solvent, the residue was purified by column chromatography (20 g of silica gel, EtOAc) to yield dimethyl-acetyl-diazomethylphosphonate **59** (1.1 g, 82.7 %) as a yellow oil.

d: 1.2 (g/mL);

R_f: 0.6 (silica gel, EtOAc);

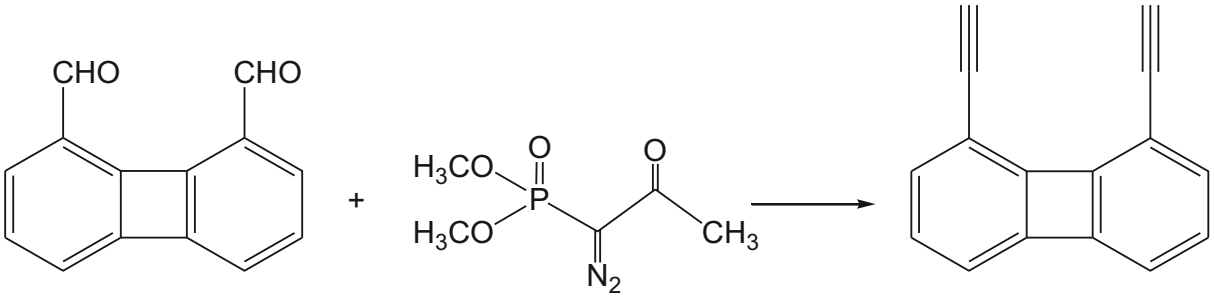
^{1}H-NMR (200 MHz, $CDCl_3$): δ = 2.27 (s, 3H, C**H**$_3$C=O), 3.82 (s, 3H, C**H**$_3$O), 3.88 ppm (s, 3H, C**H**$_3$O);

MS (EI, 70 eV, 200 °C): m/z (% relative intensity) = 192 (22) $[M]^+$, 164 (12) $[M\text{-}N_2]^+$, 150 (8) $[M\text{-}CH_2CO]$, 130 (10) $[M\text{-}CH_2O\text{-}CH_3]^+$, 93 (100) $[M\text{-}(CH_3O)_2PO]^+$, 79 (28) $[M\text{-}CH_3CON_2\text{-}CH_2O]^+$, 63 (14), 47 (12), 43 (19);

BRN: 10426989;

CAS-No: 90965-06-3.

5.3.9 Synthesis of 1,8-diethynylbiphenylene (10)



58 $C_{14}H_8O_2$ 208.22

59 $C_5H_9O_4P$ 192.11

10 $C_{16}H_8$ 200.24

To a solution of 1,8-diformylbiphenylene **58** (80 mg, 0.38 mmol) and K_2CO_3 (203 mg, 1.52 mmol, 4 eq.) in 8 mL MeOH* was injected dimethyl-acetyl-diazomethylphosphonate **59** (0.13 mL, 0.81 mmol, 2 eq.) of through a septum cap. The reaction mixture was stirred for 4 hours at room temperature. The reaction was quenched by sat. $NaHCO_3$ solution and the resulting mixture was extracted several times with 15 mL diethyl ether. The combined organic phases were washed through a plug of cotton and concentrated by rotary evaporator. The residue was purified by column chromatography (1 cm column) (10 g of silica gel, PE/CH_2Cl_2 2:1) yield 1,8-diethynylbiphenylene **10** (62 mg, 80.1 %) as light yellow crystals.

Mp: 128 °C;

R_f: 0.6 (silica gel, CH_2Cl_2/PE 2:1);

IR (KBr) $\tilde{\nu}$ =3283 (m, C≡C-H), 2148 (w, C≡C-), 1448 (m), 1385 (m), 1271(m), 1197 (m), 973 (w), 888 (w), 769 (s, Aryl-H), 703 (m, CH), 654 (m), 625 cm^{-1} (s);

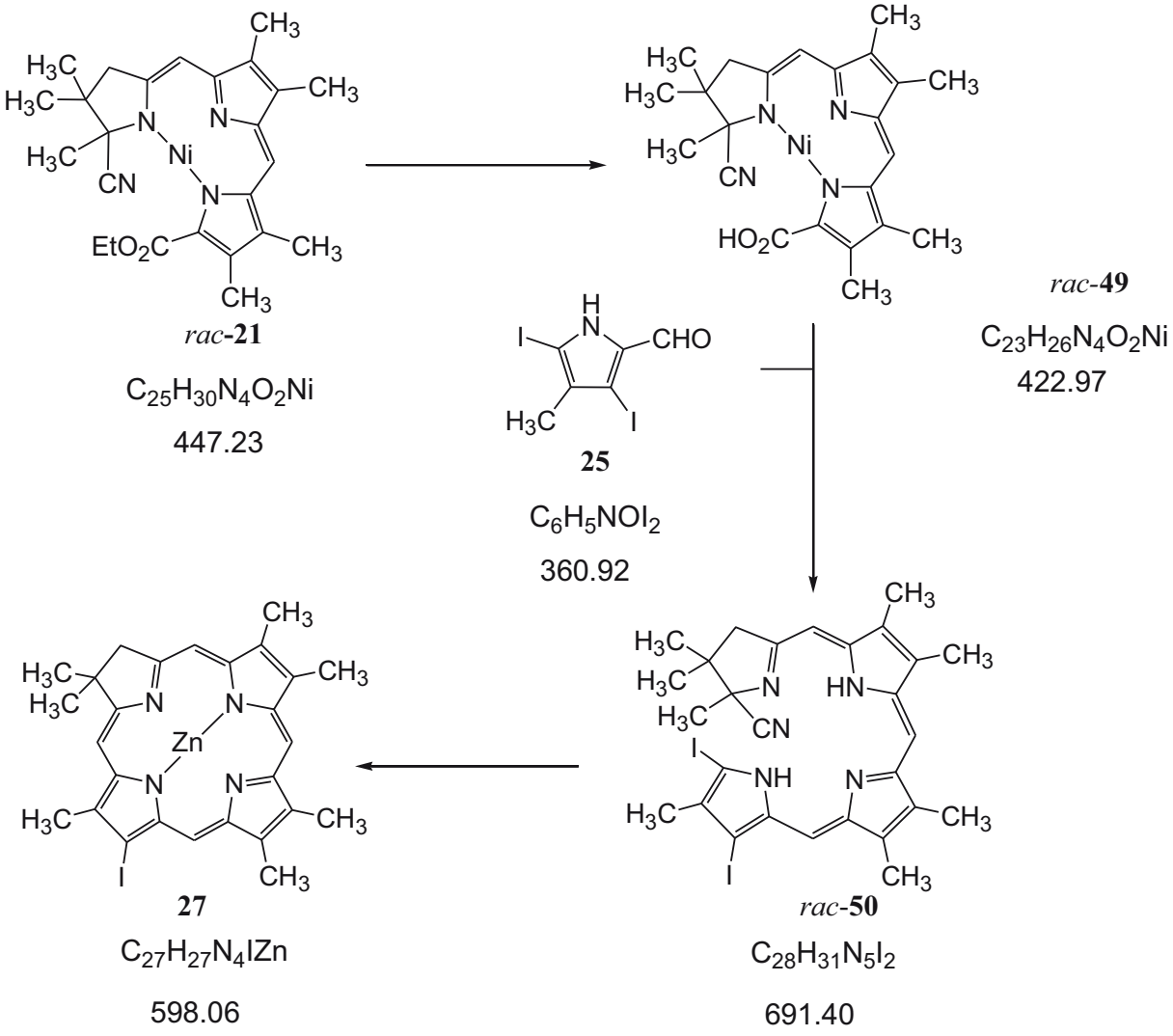
^{1}H-NMR (200 MHz, $CDCl_3$): δ = 3.15 (s, 2H, 1,8-CC**H**), 6.60 (d, ^{3}J = 6.2 Hz, 2H, 4,5-C**H**), 6.78 (dd, ^{3}J = 6.9 Hz, ^{3}J = 8.3 Hz, 2H, 3,6-C**H**), 6.84 ppm (d, ^{3}J = 8.3 Hz, 2H, 2,7-C**H**);

MS (EI, 70 eV, 200 °C): m/z (% relative intensity) = 200 (100) $[M]^+$, 199 (21) $[M-H]^+$, 150 (3) $[M-C_4H_2]$, 100 (10) $[M-C_8H_4]$, 87 (4), 74 (2);

HR-MS [EI, $C_{16}H_8$, R ≈ 10000]: Calculated: 200.06260;
Measured: 200.06325.

5.4 SYNTHESIS OF A "*TRANS*"-CHLORIN DYAD

5.4.1 Synthesis of [2,3-dihydro-17-iodo-2,2,7,8,12,13,18-heptamethyl-porphinato]-zinc(II) (27)[52,57]



To a solution of nickel complex *rac*-**21** (10.0 mg, 0.021 mmol) in 3 mL of THF* was added a solution of 5 N KOH in MeOH/H_2O (9:1) (1.6 mL, 8 mmol). The reaction mixture was heated to 70 ^oC for 45 minutes. After cooling, the solution was treated with 10 mL of sat. aq. $NaHCO_3$ solution then extracted 3 times with portions of CH_2Cl_2 (10 mL). The combined organic phase was filtered through a plug of cotton, concentrated under reduced pressure and dried on an oil pump to yield acid *rac*-**49**. To a solution of crude acid *rac*-**49** (8.2 mg, 0.019 mmol) and diiodopyrrole **25** (11.35 mg, 0.03 mmol, 1.5 eq.) in 6 mL of $CHCl_3$* was added a solution of 0.4 N *p*-toluenesulfonic acid in $CHCl_3$* (4 mL, 1.6 mmol). The reaction mixture

was stirred for 2.5 hours at rt.. The solution was then treated with 10 mL of sat. aq. $NaHCO_3$ solution and extracted 3 times with 10 mL portions of CH_2Cl_2. The combined organic phases were filtered through a plug of cotton and concentrated. The resulting solid was purified by column chromatography (10 g of neutral Al_2O_3 10 g, CH_2Cl_2) to afford tetracycle *rac*-**50** (10.27 mg, 67 %) as a blue-green solid. To a solution of crude teracycle *rac*-**53** and $Zn(CH_3COO)_2$ (19.7 mg, 0.11 mmol, 5 eq.) in 3 mL of sulfolane was added 0.8 mL of DBU. The reaction mixture was heated to 80 ^oC for 3 hours. After cooling, the solution was treated with 10mL of sat. aq. $NaHCO_3$ solution then extracted 3 times with 10 mL portions of CH_2Cl_2. The organic extract was concentrated using kugelrohr distillation at 110 ^oC. The residue was purified by column chromatography (10 g silica gel, CH_2Cl_2) to afford chlorin **27** (6.7 mg, 0.011 mmol, 53 %) as a green solid.

Mp: 280 ^oC (chloroform, decomposition);

R_f: 0.55 (silica gel, PE/acetone, 3:1);

IR (KBr): $\tilde{\nu}$ = 2944 (w, CH_3), 2911 (m, CH_3), 2849 (w, CH_3), 1614 (s, C=C), 1559 (m), 1586 (m), 1559 (m), 1458 (w), 1309 (w), 1221 (w)1194 (m), 1127 (s), 1032 (s), 890 (m), 816 (w), 744 (s), 708 10 cm^{-1} (m);

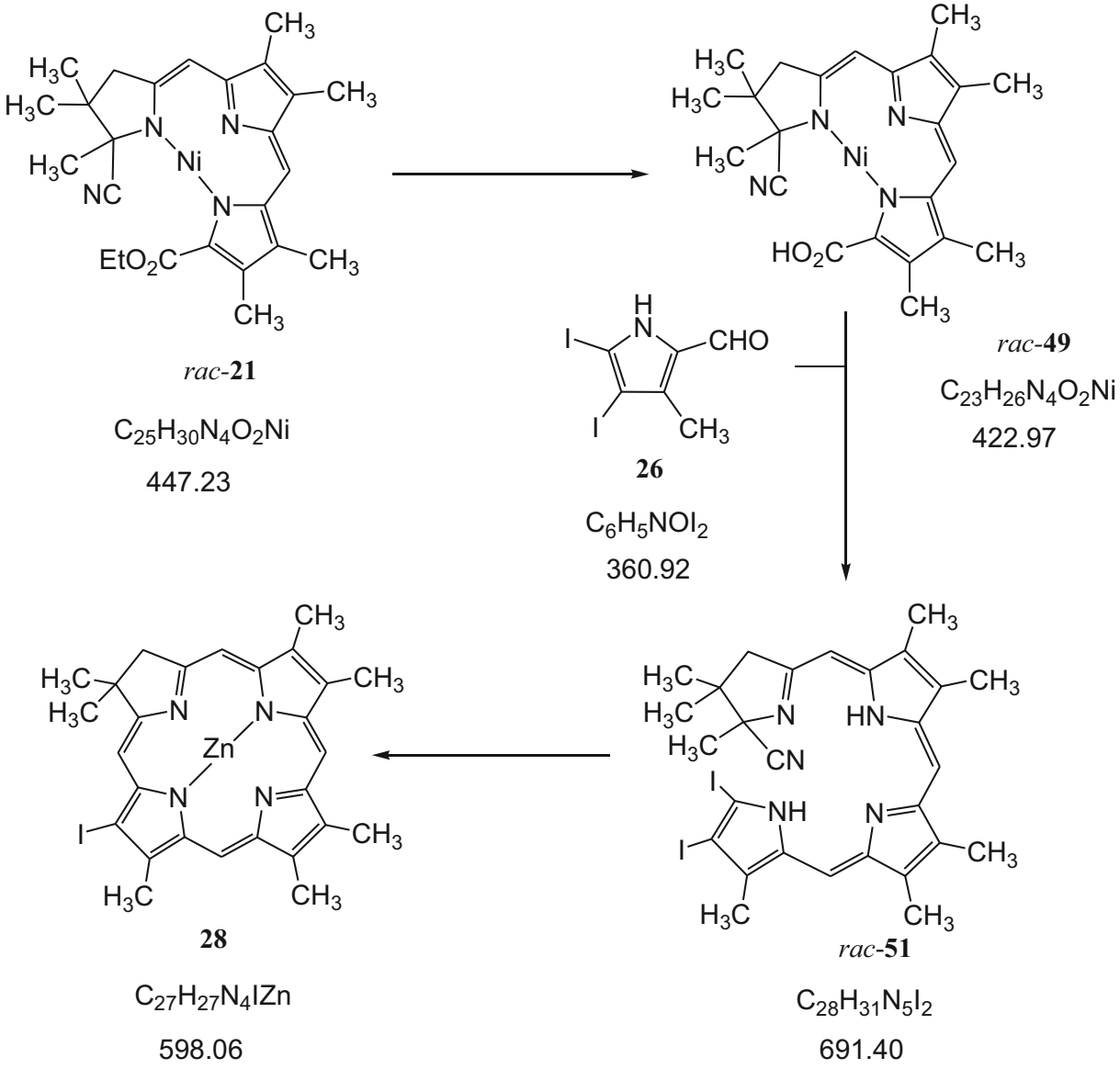
UV/ VIS (acetone): λ_{max} (ε) = 625 (42457), 575 (2795), 505 (1242), 400 (98447), 320 nm (38198 cm^2mmol^{-1});

^{1}H-NMR (200 MHz, C_6D_6/D_5 pyridine): δ = 1.78 (s, 6H, 2*2-C**H**$_3$), 3.18, 3.21, 3.24, 3.28, (4 s, 12H, 7-, 13-, 8-, 12-, C**H**$_3$), 3.36 (s, 3H, 18-C**H**$_3$), 4.21 (s, 2H, 3-C**H**$_2$), 8.57, 8.66, 9.65, 10.13 ppm (4s, 4H, 5-, 20-, 10-, 15-C**H**);

MS (ESI, positive, MeOH): 598 $[M]^+$, 621 $[M+Na]^+$; (ESI, negative, MeOH): 597 $[M-H]^-$;

HR-MS [EI, $C_{27}H_{27}N_4IZn$, R ≈ 10000]: Calculated: 598.05719;
Measured: 598.05862.

5.4.2 Synthesis of [2,3-dihydro-18-iodo-2,2,7,8,12,13,17-heptamethyl-porphinato]-zinc(II) (27)[52,57]



To a solution of nickel complex *rac*-**21** (10.0 mg, 0.021 mmol) in 3 mL of THF* was added a solution of 5 N KOH in MeOH/H_2O (9:1) (1.6 mL, 8 mmol). The reaction mixture was heated to 70 °C for 45 minutes. After cooling, the solution was treated with 10 mL of sat. aq. $NaHCO_3$ solution then extracted 3 times with 10 mL portions of CH_2Cl_2. The combined organic layers were filtered through a plug of cotton, concentrated and dried over an oil pump to yield acid *rac*-**49**. To a solution of crude acid *rac*-**49** (8 mg, 0.019 mmol) and diiodopyrrole **26** (11.35 mg, 0.03 mmol, 1.5 eq.) in 6 mL of $CHCl_3$* was added a solution of 0.4 N *p*-toluenesulfonic acid in $CHCl_3$* (4 mL, 1.6 mmol). The reaction mixture was stirred for 2.5 hours at room temperature. The solution was then treated with 10 mL of sat. aq. $NaHCO_3$

solution, extracted 3 times with 10 mL portions of CH_2Cl_2. The combined organic phases were filtered through a plug of cotton and concentrated. The resulting solid was purified by chromatography (10 g of neutral Al_2O_3, CH_2Cl_2) to afford tetracycle *rac*-**51** as a blue-green solid. To a soluion of teracycle *rac*-**51** (9.5 mg, 62 %) and $Zn(CH_3COO)_2$ (19.7 mg, 0.11 mmol, 5 eq.) in 3 mL of sulfolane was added 0.8 mL of DBU. The reaction mixture was heated to 80 °C for 3 hours. After cooling, the solution was treated with 10 mL of sat. aq. $NaHCO_3$ solution then extracted 3 times with 10 mL portions of CH_2Cl_2. The organic extract was concentrated using kugelrohr distillation at 110 °C. The residue was purified by column chromatography (10 g of silica gel, CH_2Cl_2) to afford chlorin **28** (6.2 mg, 0.01 mmol, 49 %) as a green solid.

Mp: 280 °C (decomposition);

R_f: 0.6 (silica gel, PE/acetone, 3:1);

IR (KBr): $\tilde{\nu}$ = 2949 (w, CH_3), 2916 (m, CH_3), 2848 (w, CH_3), 1625 (C=C), 1585 (m), 1586 (m), 1559 (m), 1456 (w), 1389 (w), 1220 (w), 1193 (m), 1139 (m), 1051 (s), 943 (m), 842 (w), 740 (s), 708 cm^{-1} (m);

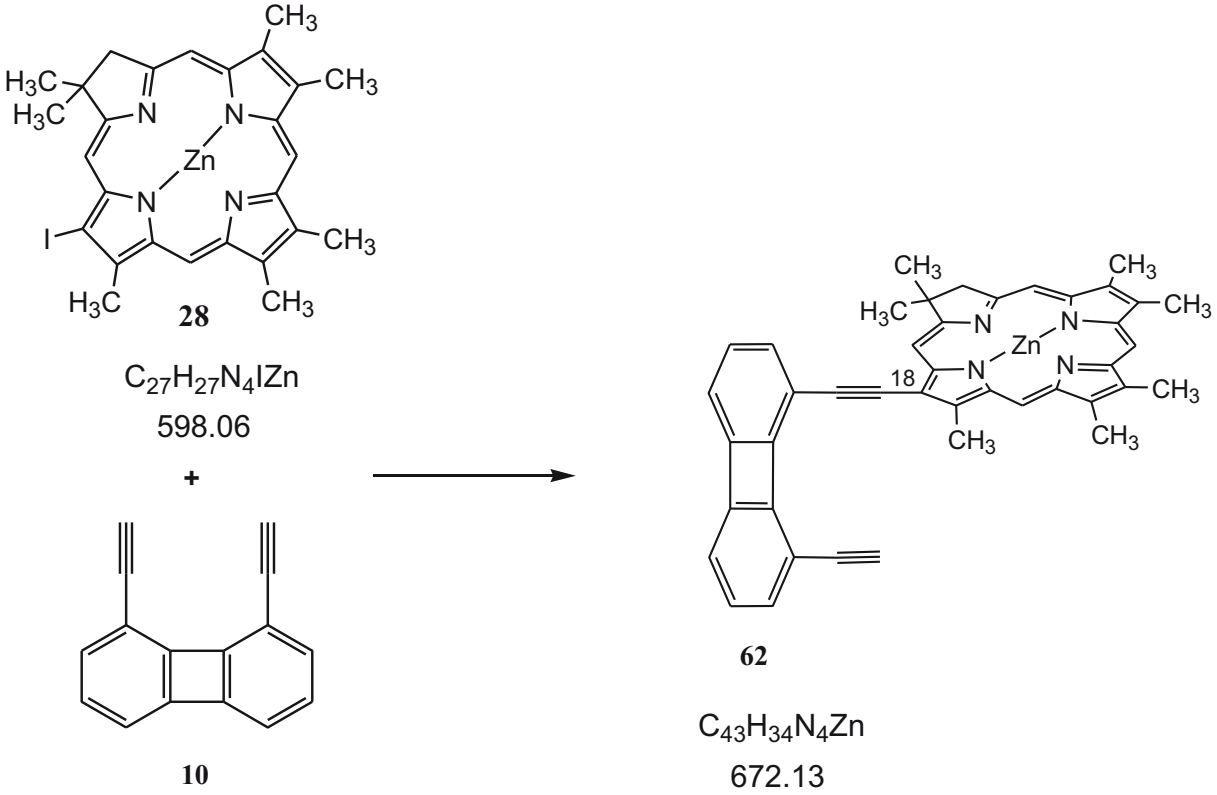
UV/ VIS (acetone): λ_{max} (ε) = 620 (44225), 575 (5633), 510 (21818), 400 (108450), 325 nm (23943 cm^2mmol^{-1});

^{1}H NMR (360 MHz, C_6D_6): δ = ^{1}H NMR (360 MHz, C_6D_6) δ = 1.87 (s, 6H, 2*2-C**H**$_3$), 3.13, 3.19, 3.21, 3.23, (4s, 12H, 7-, 13-, 8-, 12-C**H**$_3$), 3.43 (s, 3H, 17-C**H**$_3$), 4.10 (s, 2H, 3-C**H**$_2$), 8.47, 8.90, 9.48, 10.54 ppm (4s, 4H, 5-, 20-, 10-, 15-C**H**);

MS (ESI, positive, MeOH): 597 $[M-H]^-$, 629 $[M+CH_3O^-]$;

HR-MS [EI, $C_{27}H_{27}N_4IZn$, R ≈ 10000]: Calculated: 598.05719;
Measured: 598.05798.

5.4.3 Synthesis of [5,6-dihydro-1-(8'-ethynyl-1'-naphthalylethynyl)-5,5,10,11,15,16,20-heptamethyl-porphinato]-zinc(II) (62)



To a solution of 18-iodochlorin **28** (10.2 mg, 0.017 mmol) and 1,8-diacetylenbiphenylen (10.0 mg, 0.05mmol, 3 eq.) in 5 mL of Toluene/TEA (5:1) was added $Pd_2(dba)_3$ (2.60 mg, 2.84 µmol) and $P(o\text{-}tol)_3$ (5.2 mg, 0.017 mmol). The mixture was heated to 60 °C under argon atmosphere. After 7 hours, the mixture was concentrated under reduced pressure and the residue was purified by column chromatography (10 g of silica gel, PE/acetone 3:1) to afford **62** (1.3 mg, 11.4 %) as a green solid.

Mp: 230 °C (chloroform) (decomposition);

R_f: 0.4 (silica gel, PE/acetone, 3:1);

IR (KBr): $\tilde{\nu}$ = 2922 (s), 2850 (w, CH_3), 3437 (s, -C≡C-H), 2360 (w, -C≡C-), 1624 (m), 1459 (w), 1389 cm^{-1} (w) ;

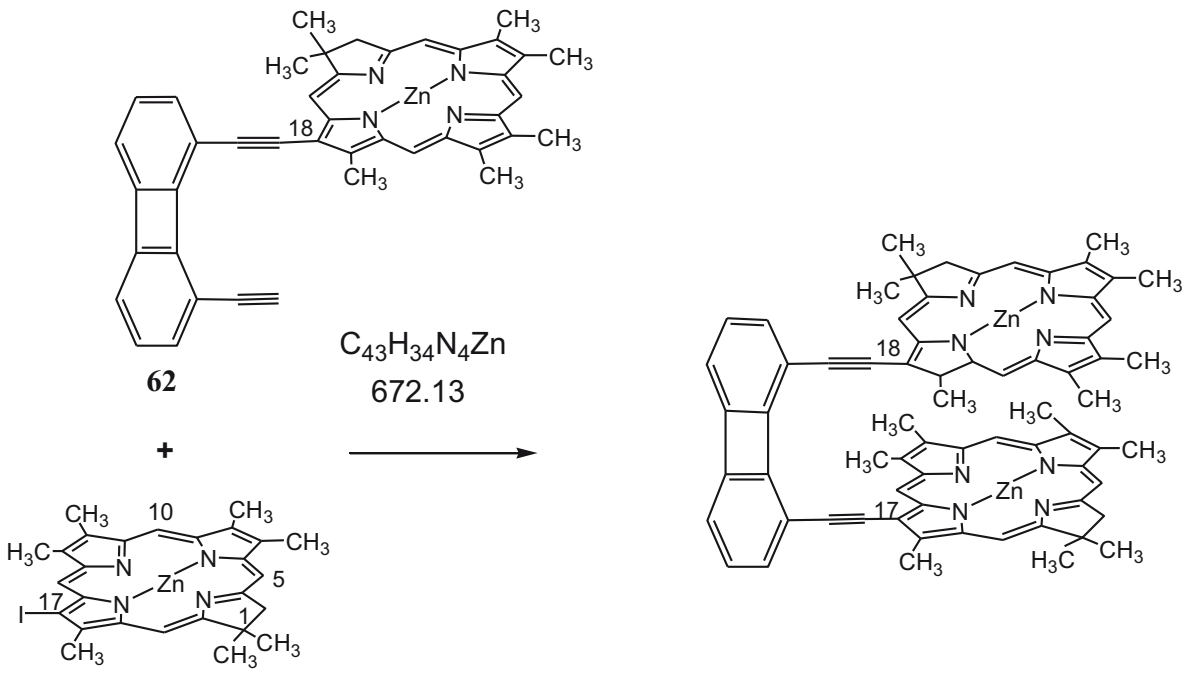
UV/ VIS (acetone): λ_{max} (ε)= 635 (59885), 590 (6303), 505 (2292), 405 (102292), 325 nm (28653 cm^2mmol^{-1});

^{1}H NMR (360 MHz, C_6D_6): δ=1.87 ppm (s, 6H, 2*5-C**H**$_3$), 2.72 (s, 1H, 8'-C**H**), 3.12 (s, 3H, 10-C**H**$_3$), 3.21(s, 3H, 11-C**H**$_3$), 3.26 (s, 3H, 16-C**H**$_3$), 3.29 (s, 3H, 15-C**H**$_3$), 3.63 (s, 3H, 20-C**H**$_3$), 4.10 (s, 2H, 6-C**H**$_2$), 6.25 (d, ^{3}J = 6.9 Hz, 1H, 5'-C**H**$_{Ar}$), 6.31 (d, ^{3}J = 6.7 Hz, 1H, 4'-C**H**$_{Ar}$), 6.36 (dd, ^{3}J = 7.5 Hz, 3J = 6.8 Hz, 1H, 6'-C**H**$_{Ar}$), 6.56 (dd, ^{3}J = 7.5 Hz, 3J = 0.79 Hz, 1H, 3'-C**H**$_{Ar}$), 6.78 (d, ^{3}J = 0.83, 1H, 7'-C**H**$_{Ar}$), 7.25(d, ^{3}J = 8.1 Hz, 1H, 2'-C**H**$_{Ar}$), 8.46 (s, 1H, 5=C**H**), 9.16 (s, 1H, 20=C**H**), 9.51 (s, 1H, 10=C**H**), 9.66 ppm (s, 1H, 15=C**H**);

MS (ESI, positive, MeOH): 670 $[M]^+$; (ESI, negative, MeOH): 705 $[M+Cl]^-$;

HR-MS [MALDI, $C_{43}H_{34}N_4Zn$, R ≈ 7000]: Calculated: 670.2069;
Measured: 670.2045.

5.4.4 Synthesis of cofacial chlorin dyad (64)



To a solution of **62** (5 mg, 7.4 μmmol) and iodochlorin **27** (5 mg, 8.3 μmol) in 3 mL of toluene/TEA (5:1) was added $Pd_2(dba)_3$ (1.3 mg, 1.4 μmol) and $P(o\text{-}tol)_3$ (3 mg, 9.8 μmol). The reaction mixture was heated to 60 ^oC under argon atmosphere for 7 hours. After concentrated, the residue was purified firstly on the column chromatography (10 g silica gel, PE/acetone 3:1). The fraction containing the product was continuously chromatographed (10 g silica gel, PE/acetone/methanol 4:1:0.5) to afford cofacial chlorin dyad **64 (**0.9 mg, 10 %) as a green solid.

R_f: 0.6 (silica gel, PE/acetone/methanol 4:1:0.5);

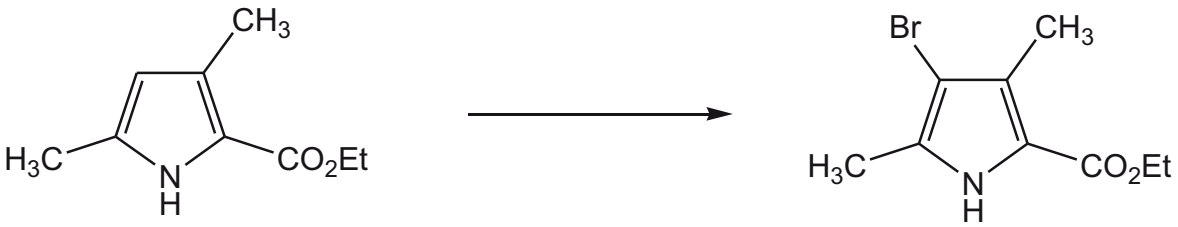
UV/Vis (methanol): λ_{max} (ε) = 640 (88857), 515 (8000), 395 nm (172000 cm^2mmol^{-1});

MS (ESI, positive, MeOH**)**: 1140 $[M]^+$;

HR-MS [MALDI, $C_{70}H_{60}N_8Zn_2$, R≈7000]**:** Calculated: 1140.3518;
Measured: 1140.3512.

5.5 STUDY DIRECTED TO 12-BROMO-2,2,7,8,13,17,18-HEPTALMETHYLCHLORIN

5.5.1 Synthesis of ethyl 4-bromo-3,5-dimethyl-1*H*-pyrrole-2-carboxylate (66)



65

$C_9H_{13}O_2N$

166.11

66

$C_9H_{12}O_2NBr$

246.09

To a solution of pyrrole **65** (139 mg, 0.84 mmol) in 6 mL of THF* cooled to -78 °C was added a solution of NBS (149 mg, 0.84 mmol, 1 eq.) in 10 mL of THF* through a septum cap. After 1 hour, the cooling bath was removed. The reaction mixture was diluted with 20 ml of dichlomethane and quenched by addition of 30 mL of sat. aq. $NaHCO_3$ solution. The mixture was separated and the aqueous phase was extracted twice with 20 mL portions of dichlomethene. The combined organic phases were concentrated under reduced pressure. The resulting residue was purified by column chromatography (20 g of silica gel, CH_2Cl_2). The crude product was recrystallized from THF/n-hexan to yield ethyl 4-bromo-3,5-dimethyl-1***H***-pyrrole-2-carboxylate **66** (114.1 mg, 70.18 %) as a colourless solid.

Mp: 148 °C (THF/n-hexan);

R_f: 0.6 (silica gel, CH_2Cl_2);

IR (KBr): $\tilde{\nu}$ = 3304 (s, NH), 2990 (w, CH-alkyl) , 2922 (w, C-H, alkyl) 1674 (s, C=O), 1445 (m), 1270 (s), 1215 (s), 1121 (m), 1023 (m), 767 (m), 685 (w), 618 cm^{-1} (w);

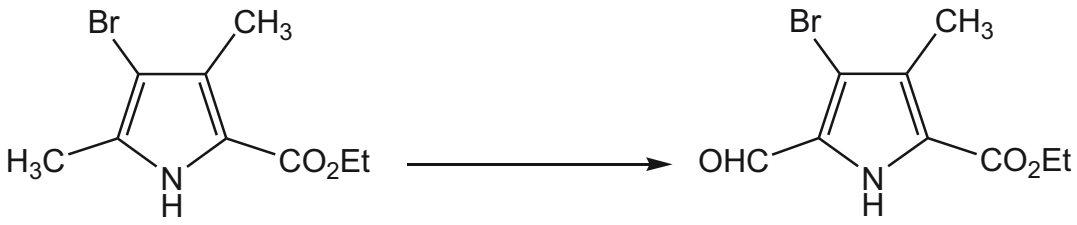
^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.37 (t, ^{3}J = 7.1 Hz, 3H, $CH_2C\mathbf{H}_3$), 2.30 (s, 3H, 5-$\mathbf{CH}_3$), 2.37 (s, 3H, 3-$C\mathbf{H}_3$), 4.32 (q, 3J = 7.3 Hz, 2H, $OC\mathbf{H}_2$), 8.7 (s, 1H, N**H**);

MS (EI, 70 eV, direct, T = 200 °C): m/z (% rel. intensity) = 247 (88) [M, $^{79}Br]^+$, 245 (92) [M, $^{81}Br]^+$, 121 (100) [M, ^{81}Br - $C_2H_5OH]^+$, 199 (100) [M,^{79}Br - $C_2H_5OH]^+$, 120 (12) [M - $C_2H_5OH^{79}Br]^+$, 92 (40) [M - $C_3H_6O_2{}^{79}Br]^+$, 65(28);

BRN: 142633;

CAS-No: 5408-07-1.

5.5.2 Synthesis of ethyl 4-bromo-5-formyl-3-methyl -1*H*-pyrrole-2-carboxylate (29)



66

$C_9H_{12}O_2NBr$

246.09

29

$C_9H_{10}O_3NBr$

260.07

To a solution of pyrrole **66** (1.03 g, 4.2 mmol) in 30 mL of $CHCl_3$* was added $Pb(CH_3COO)_4$ (1.86 g, 4.2 mmol, 1 eq.). The mixture was refluxed for 1 hour. $Pb(CH_3COO)_4$ (2.80 g, 6.3 mmol, 1.5 eq.) was then added and the reaction mixture was refluxed for further16 hours. After cooling, the solid was removed by a pad of celite and the filtrate was then added with ethylene glycol (0.3 mL, 5mmol). The resulting mixture was stirred for 20 min. and then washed with 10 mL of sat. aq. NaCl solution to separate the organic phase. The aqueous phase was extracted twice with 20 mL portions of CH_2Cl_2. The combined organic phases were concentrated to yield the crude diacetate. This intermediate product was then dissolved in THF (20 mL) and hydrolyzed with 25 mL of HCl (2.5 M) at rt. for 4 hours. 100 mL of sat. aq. NaCl solution was then added to separate the organic phase. The aqueous phase was continuously extracted twice with 30 mL portions of CH_2Cl_2. The combined extracts were washed with sat. aq. $NaHCO_3$ solution and the solvent was removed by rotary evaporator. The crude product was purified by column chromatography (50 g of silica gel, CH_2Cl_2/EtOAc 20:1) and recrystallized from $CHCl_3$/n-pentan) to yield formylpyrrole **29** (673.2 mg, 62.3 %) as colourless crystals.

Mp: 135 °C ($CHCl_3$/n-pentane);

R_f: 0.6 (silica gel, CH_2Cl_2/EtOAc 20:1);

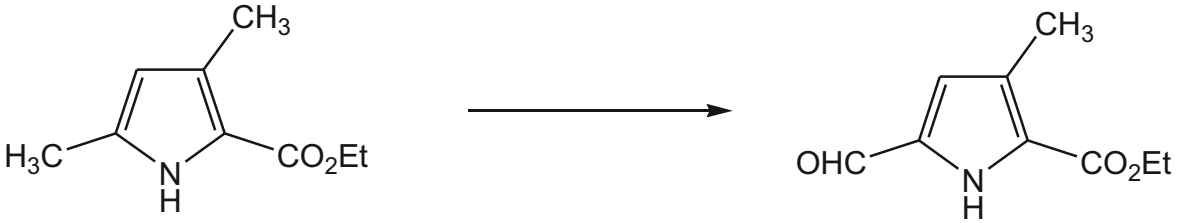
IR (KBr): $\tilde{\nu}$ = 3248 (s, NH), 2980 (w, CH-alkyl) , 2931 (w, C-H, alkyl), 1698 (s, C=O, aldehyde), 1668 (s, C=O, ethylester) 1546 (m), 178 (m), 1438 (m), 1258 (s), 1101 (m), 1014 (m), 773 (s), 637 (w), 606 cm^{-1} (w);

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.42 (t, ^{3}J = 7.1 Hz, 3H, $CH_2C\mathbf{H}_3$), 2.34 (s, 3H, $C\mathbf{H}_3$), (s, 3H, $C\mathbf{H}_3$), 4.39 (q, 3J = 7.3 Hz, 2H, $OC\mathbf{H}_2$), 9.73 (s, 1H, C**H**O);

MS (EI, 70 eV, direct, T = 200 °C): m/z (% rel. intensity) = 261 (98) [M, ^{81}Br]$^+$, 259 (100) [M, ^{79}Br]$^+$, 232 (56) [M, ^{81}Br - CHO]$^+$, 230 (56) [M,^{79}Br - CHO]$^+$, 216 (82) [M, ^{81}Br - $C_2H_5O]^+$, 215 (65) [M, ^{81}Br - $C_2H_5OH]^+$, 214 (84) [M,^{79}Br - $C_2H_5O]^+$, 213 (58) [M,^{79}Br - $C_2H_5OH]^+$, 187 (40) [M, ^{81}Br - $C_3H_6O_2]^+$, 185 (36) [M, ^{79}Br - $C_3H_6O_2]^+$, 106(38) [M, - $C_3H_6O_2{}^{79}Br]^+$, 78 (20), 51 (23);

BRN: 176617.

5.5.3 Synthesis of ethyl 5-formyl-3-methyl-1*H*-pyrrole-2-carboxylate (67)



65

$C_9H_{13}O_2N$

166.11

67

$C_9H_{11}O_3N$

181.19

To a solution of dimethylpyrrole **65** (520 mg, 3.1 mmol) in 20 mL of $CHCl_3$* was added $Pb(CH_3COO)_4$ (1.4 g, 3.1 mmol, 1 eq.). The mixture was refluxed for 60 minutes. $Pb(CH_3COO)_4$ (2.1 g, 4.6 mmol, 1.5 eq.) was then added and the reaction mixture was refluxed for 16 hours. After cooling, the solid was removed by a pad of celite and the filtrate

was then treated with ethylene glycol (0.3 mL, 5mmol). The resulting mixture was stirred for 20 min. then washed with 10 mL of sat. aq. NaCl solution to separate the organic phase. The aqueous phase was extracted twice with 20 mL portions of CH_2Cl_2. The combined organic phases were concentrated to yield a crude diacetate. This intermediate product was then dissolved in 15 mL of THF and hydrolyzed with 20 mL of HCl (2.5 M) at rt. for 4 h.. 100 mL of sat. aq. NaCl solution was then added to separate the organic phase. The aqueous phase was continuously extracted twice with 30 mL portion of CH_2Cl_2. The combined extracts were washed with 30 mL of sat. aq. $NaHCO_3$ solution and the solvent was removed by rotary evaporator. The residue was purified by column chromatography (50 g of silica gel, CH_2Cl_2/EtOAc 20:1) and recrystallized from $CHCl_3$/n-pentan to yield formylpyrrole **67** (351 mg, 62.0 %) as colourless crystals.

Mp: 106 ^oC ($CHCl_3$/n-pentane);

R_f: 0.6 (silica gel, CH_2Cl_2/EtOAc 20:1);

IR (KBr): $\tilde{\nu}$ = 3273 (s, NH), 2975 (w, CH-alkyl), 1674 (s,br C=O, aldehyde, C=O, ethylester) 1546 (m), 1485 (s), 1382 (m), 1323 (s), 1261 (s), 1143 (s), 1123 (m), 1102 (m), 1018 (s), 871 (m), 821 (s), 777 (m), 760 (s), 726 (m), 674 (w), 632 cm^{-1} (w);

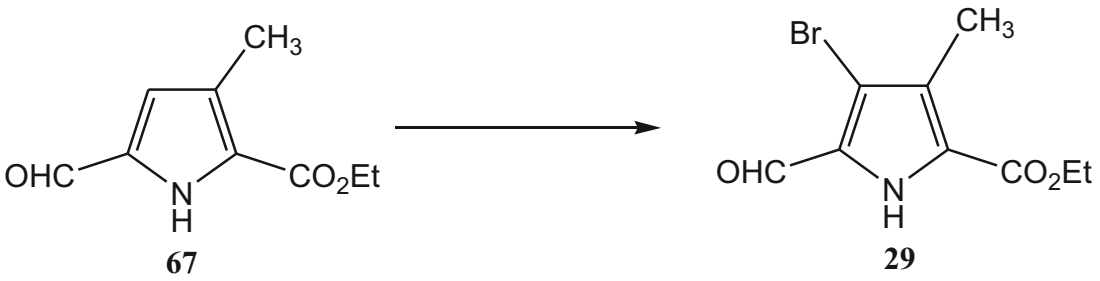
^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.40 (t, ^{3}J = 7.2 Hz, 3H, CH_2-C**H**$_3$), 2.39 (s, 3H, C**H**$_3$), 4.40 (q, ^{3}J = 7.2 Hz, 2H, C**H**$_2$CH$_3$), 6.76 (s, 1H, H), 9.61 (s, 1H, C**H**O);

MS (EI, 70 eV, Direkteinlass, T = 200°C): m/z (% relative Intensität) = 181 (100) $[M]^+$, 152 (69) $[M - CHO]^+$, 136 (45) $[M - C_2H_5O]^+$, 134 (52), 107 (35) $[M - C_3H_6O_2]^+$, 80 (6), 78 (6);

BRN: 156188;

CAS: 26018-30-4.

5.5.4 Synthesis of ethyl 4-bromo-5-formyl-3-methyl -1*H*-pyrrole-2-carboxylate (29)



67 **29**

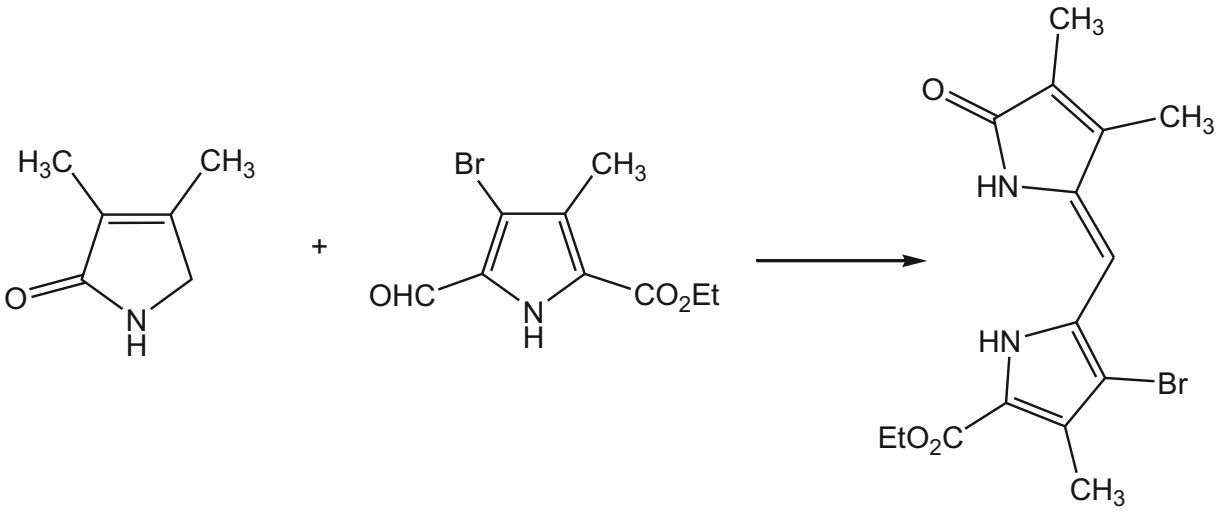
$C_9H_{11}O_3N$ $C_9H_{10}O_3NBr$

181.19 260.07

A solution of pyrrole **67** (181 mg, 1 mmol) in 6 mL of THF* was cooled to -78 ^oC and 178 mg NBS (1 mmol, 1 eq.) NBS in 10 mL of THF* was then added through a septum cap. After 1 hour, the reaction mixture was diluted with 20 ml of dichlomethane and quenched by addition of 30 ml of sat. aq. $NaHCO_3$ solution. The mixture was separated and the aqueous phase was extracted twice with 20 mL portions of dichlomethane. The combined organic phase was concentrated by rotary evaporator. The resulting residue was purified by column chromatography (20 g of silica gel, CH_2Cl_2). The crude product was recrystallized from (THF/n-hexane) to yield bromopyrrole **29** (31 mg, 12 %) as a colourless solid.

For characterization: see **5.5.2**

5.5.5 Synthesis of ethyl 5-(1,5-dyhidro-3,4-dimethyl-5-oxo-1*H*-pyrrole-2-ylidenmethyl)-4-bromo-3-methyl-1*H*-pyrrole-2-carboxylate (68)



14	**29**	**68**
C_6H_9ON	$C_9H_{10}O_3NBr$	$C_{15}H_{17}O_3N_2Br$
111.14	260.07	353.21

To a solution of pyrrolinone **14** (19.92 mg, 0.179 mmol, 1 eq.) and pyrrole **29** (56 mg, 0.215 mmol, 1.2 eq.) in 7 mL of benzene was added DBU (75 µL, 0.258 mmol, 1.45 eq.). The mixture was connected to the soxhlet apparatus containing molecular sieve (3 Å) and refluxed for 17 hours. After cooling, the reaction mixture was washed with 20 mL of sat. aq. $NaHCO_3$ solution and extracted 3 times with 20 mL portions of CH_2Cl_2. The combined organic extract was filtered through a plug of cotton and the solvent was removed by rotary evaporator. The resulting crude product was purified on the column chromatography (20 g of silica gel, CH_2Cl_2/EtOAc: 3:1) to afford bicycle **68** (44.6 mg, 32.9 %) as a pale yellow solid.

Mp: 270 ^oC ($CHCl_3$);

R_f: 0.3 (silica gel, CH_2Cl_2/EtOAc 3:1);

IR (KBr): $\tilde{\nu}$ = 3238 (m, br, NH), 2981 (w, CH-alkyl) , 2919 (w, C-H, alkyl), 1713 (s, C=O, lactam), 1681 (s, C=O, ethylester) 1615 (m), 1615 (m), 1452 (m), 1280 (s), 1222 (m), 1070 (m), 1119 (m), 1024 (w), 755 (w), 695 cm^{-1} (w);

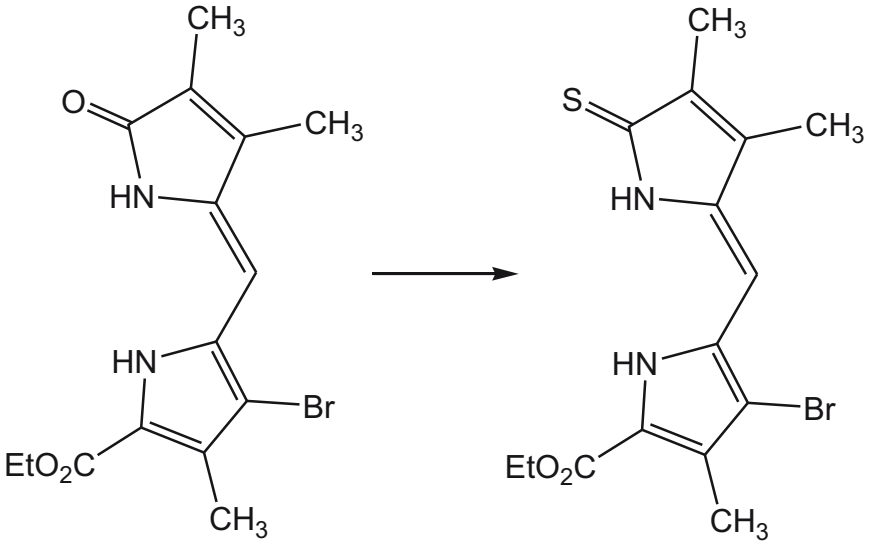
UV/ VIS (methanol): λ_{max} (ε) = 400 (28480), 375 (30062), 254.9 nm (23048 cm^2mmol^{-1});

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.37 (t, ^{3}J = 7.1 Hz, 3H, $CH_2C\mathbf{H}_3$), 1.95 (s, 3H, 3-C**H**$_3$), 1,95 (s, 3H, 4-C**H**$_3$), 2.33 (s, 3H, 10-C**H**$_3$), 4.34 (q, 3J = 7.3 Hz, 2H, OC**H**$_2$), 6.04(s, 1H, 6-C**H**), 9.00 (s, 1H, 1-N**H**), 9.67 ppm (s, 1H, 8-N**H**);

MS (EI, 70 eV, direct, T = 200 °C): m/z (% rel. intensity) = 354 (56) [M, ^{81}Br]$^+$, 352 (55) [M, ^{79}Br]$^+$, 308 (46) [M, ^{81}Br – C_2H_5OH]$^+$, 307 (45) [M,^{79}Br – C_2H_5OH]$^+$, 227 (16) [M- ^{81}Br]$^+$, 199 (100) [M- $C_3H_6O_2{}^{81}$Br]$^+$, 172 (16);

HR-MS [EI, $C_{15}H_{17}N_2O_3Br$, R ≈ 10000]: Calculated: 352.04225;
Measured: 352.04212.

5.5.6 Synthesis of ethyl 5-(1,5-dyhidro-3,4-dimethyl-5-thioxo-1*H*-pyrrole-2-ylidenmethyl)-4-bromo-3-methyl-1*H*-pyrrole-2-carboxylate (69)



68
$C_{15}H_{17}O_3N_2Br$
353.21

69
$C_{15}H_{17}O_2N_2SBr$
369.27

To a solution of bicyclic lactam **68** (200 mg, 0.56 mmol) in 10 mL of THF* was added Lawessons-Reagent (0.68 mmol, 1.2 eq.) under argon atmosphere. The mixture was stirred and warmed to 40 ^oC for 3 hours and the reaction was controlled by thin layer chromatography. After removing the solvent by rotary evaporator at rt., the oily residue was

dried on a high vacuum and purified by column chromatography (50 g of silica gel, CH_2Cl_2/EtOAc 9:1) to yield thiolactam **69** (151.56 mg, 72.5 %) as an orange solid.

Mp: 270 ^oC;

R_f: 0.75 (silica gel, CH_2Cl_2/EtOAc 9:1);

IR (KBr): $\tilde{\nu}$ = 3367 (m, br, NH), 2926 (w, CH-alkyl) , 2908 (w, C-H, alkyl), 1654 (s), 1598 (s, C=O, ethylester) 1502 (m), 1294 (s), 1258 (s), 1124 (s), 1026 (s), 954 (m), 830 (m), 687 (w), 534 cm^{-1} (w);

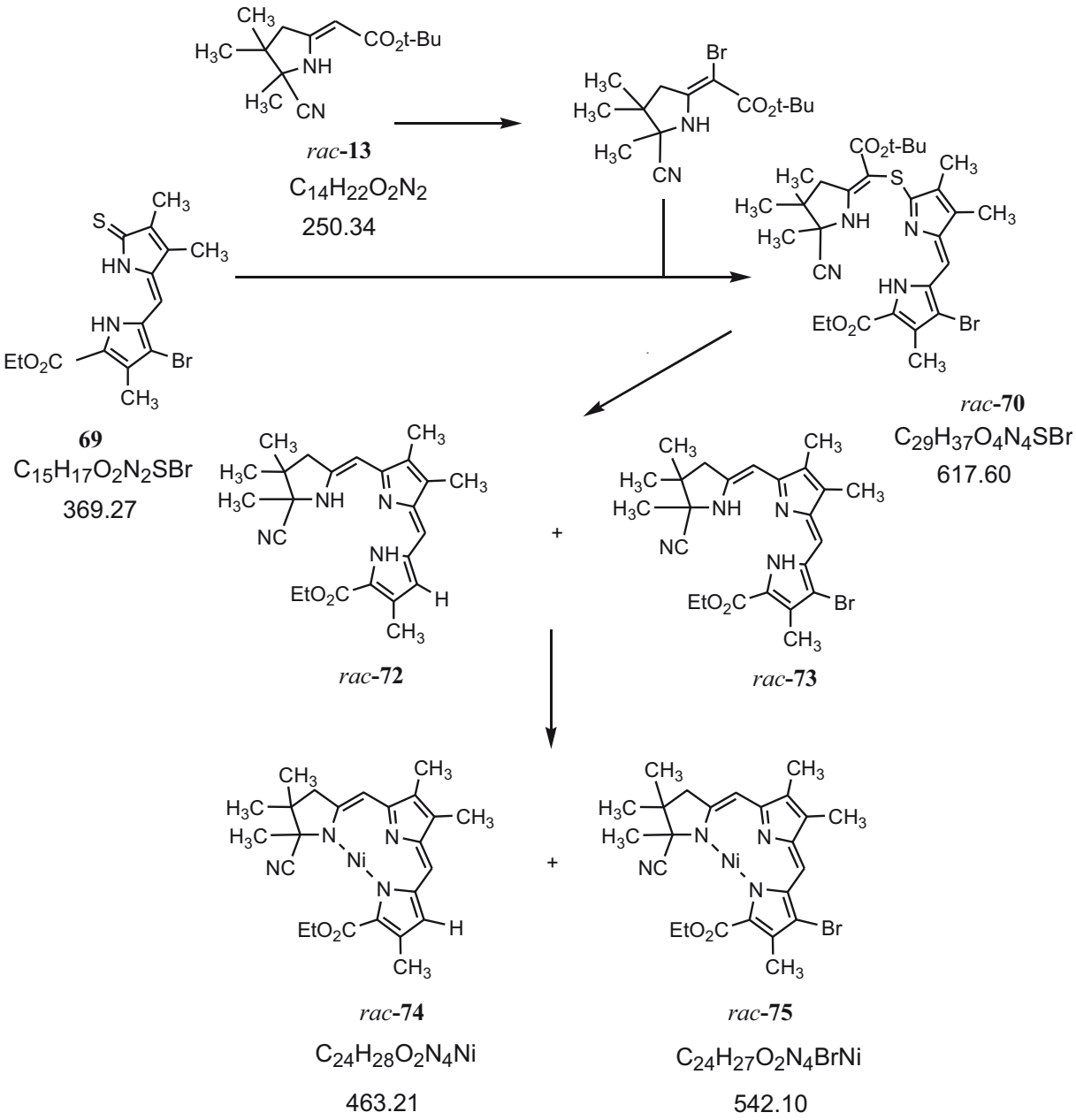
UV/ VIS (methanol): λ_{max} (ε) = 450 (27333), 280 nm (5999 cm^2mmol^{-1});

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.38 (t, ^{3}J = 7.1 Hz, 3H, -$CH_2C\mathbf{H}_3$), 2.07 (s, 3H, 3-C$\mathbf{H}_3$), 2.13 (s, 3H, 4-C$\mathbf{H}_3$), 2.33 (s, 3H, 10-C$\mathbf{H}_3$), 4.37 (q, 3J = 7.3 Hz, 2H, OC$\mathbf{H}_2$), 6.07(s, 1H, 6-C**H**), 9.47 ppm (s, s, 2H, 1-N**H**, 8-N**H,**);

MS (EI, 70 eV, direct, T = 200 °C): m/z (% rel. intensity) = 354 (56) [M, ^{81}Br]$^+$, 352 (55) [M, ^{79}Br]$^+$, 308 (46) [M, ^{81}Br – C_2H_5OH]$^+$, 307 (45) [M,^{79}Br – C_2H_5OH]$^+$, 227 (16) [M- ^{81}Br]$^+$, 199 (100) [M- $C_3H_6O_2{}^{81}$Br]$^+$, 172 (16).

HR-MS [EI, $C_{15}H_{17}N_2O_2SBr$, R ≈ 10000]: Calculated: 368.01941;
Measured: 368.01853.

5.5.7 Synthesis of [ethyl-(14*RS*)-(14-cyano-12,13,14,17-tetrahydro-2,7,8,13,13,14-hexamethyl-15*H*-tripyrrin-1-carboxylato)]nickel-(II) (74) and [ethyl-(14*RS*)-(4-bromo-14-cyano-12,13,14,17-tetrahydro- -2,7,8,13,13,14-hexamethyl-15*H*-tripyrrin-1-carboxylato)]nickel-(II) (75)



To a solution of *tert*-butylester *rac*-**13** (40.5 mg, 0.162 mmol, 1 eq.) in 8 mL of CH_2Cl_2* was added N-bromosuccinimide (31.7 mg, 0.178 mmol, 1.1 eq.). The reaction mixture was stirred in the dark and under argon atmosphere. After 30 min., the mixture of DBU (84 µL, 0.64 mmol, 4 eq.) and bicyclic thiolactam **69** (46.4, 0.152 mmol, 1 eq.) in 30 mL of CH_3CN was added and the reaction mixture was further stirred for 40 min.. The mixture was then

quenched with 20 mL of sat. aq. $NaHCO_3$ solution and extracted twice with 20 mL portions of CH_2Cl_2. The combined organic phases were concentrated under reduced pressure and the residue was purified by column chromatography (10 g of neutral Al_2O_3, CH_2Cl_2), concentrated and dried on a oil pump to afford *rac*-**70** as a yellow oil (70.53 mg, 0.11 mmol, 75.1%).

The racemic mixture *rac*-**70** was dissolved in 28 mL of benzene* together with 3 mL of trifluoroacetic acid and tris(2-cyanoethyl)phosphine (199.2 mg, 1.03 mmol, 10 eq.) . The resulting solution was refluxed for 20 min.. After cooling, the strongly red mixture was filled with 30 mL of CH_2Cl_2 and then with 20 mL of ice water. The aqueous phase was extracted twice with 10 mL portions of CH_2Cl_2. The combined organic phase was washed with 30 mL of sat. aq. $NaHCO_3$ solution and filtered through a plug of cotton and concentrated by a rotary evaporator. The crude product was purified by column chromatography (10 g of neutral Al_2O_3, CH_2Cl_2) to yield tricyclic *rac*-**72** and *rac*-**73** as organge solids in two first fractions. The crude products mixture was dried over an oil pump for the next step.

To a solution of mixture tricyclic *rac*-**72** and *rac*-**73** in 4 mL CH_2Cl_2 was added a solution of nickel(II) acetate tetrahydrate (154.4 mg, 0.63 mmol, 4 eq.) in 5 mL of MeOH and sodium acetate (200 mg, 2.4 mmol, 15 eq.) in 3 mL MeOH. After stirring at rt. for 30 min., the reaction mixture was quenched with 2 mL of CH_2Cl_2 and 5 mL of ice water. The aqueous phase was extracted twice with 5 mL portions of CH_2Cl_2. The organic phase was concentrated by a rotary evaporator and the resulting residue was purified by chromatography (10 g of neutral Al_2O_3, CH_2Cl_2/ PE 2:1) to give two fractions. Both divisions were concentrated and recrystalized from ($CHCl_3$/ n-pentane) separately. The first fraction gave the bromo substituted Ni-complex *rac*-**75** (25.3 mg, 26.2 %) as violet crystals sand the second fraction gave Nikelcomplex *rac*-**74** (6.7 mg, 9.5 %) as pink crystals.

Nickelcomplex *rac*-**74**

Mp : $\geq 280\ ^{o}C$, decomposed;

$\mathbf{R_f}$: 0.5 (aluminium oxide, CH_2Cl_2/ PE 2:1);

IR (KBr): $\tilde{\nu}$ = 2924 (w, CH_3), 2854 (CH_2), 1570 (s, C=O, ethylester), 1503 (s), 1463 (s), 1438 (m), 1384 (s), 1336 (s), 1306 (m), 1259 (w), 1175 (w), 1156 (m), 1124 (m), 1106 (m), 1012 (m), 899 (w), 827 (w), 774 (w), 726 (w), 669 (w), 629 cm^{-1} (w);

UV/ VIS (CH_2Cl_2): λ_{max} (ε) = 530 (23608), 495 (11581), 337 (21826), 295 nm (18708) cm^2mmol^{-1});

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.21 (s, 3H, 2a-C**H**$_3$), 1.28 (s, 3H, 2b-C**H**$_3$), 1.44 (t, 3H, -CH2-C**H**3), 1.77 (s, 3H, 1-C**H**$_3$), 2.06 (s, 3H, 7-C**H**$_3$), 2.16 (8-CH_3), 2.36 (s, 3H, 13-C**H**$_3$), 2.68/2.85 (AB-system, 2H, 3-C**H**$_2$), 4.60/4.68 (m, 2H, 14-CH_2C**H**$_3$), 5.52 (s, 1H, 5-C**H**), 6.31 (s, 1H, 12-C**H**)6.53 (s, 1H, 10-C**H**);

MS (ESI, positive, MeOH): 463 $[M+H]^+$, 485 $[M+Na]^+$, 501 $[M+K]^+$.

Bromo nickelcomplex *rac*-75:

Mp: ≥ 280 °C, decomposed;
R_f: 0.7 (aluminium oxide, CH_2Cl_2/ PE 2:1);

IR (KBr): $\tilde{\nu}$ = 3468 (w, br, NH), 2924 (w, CH-alkyl), 2854 (w, C-H, alkyl), 1574 (s), 1503 (s), 1462 (m), 1382 (m), 1314 (m), 1104 (m), 820 (w), 788 cm^{-1} (w);

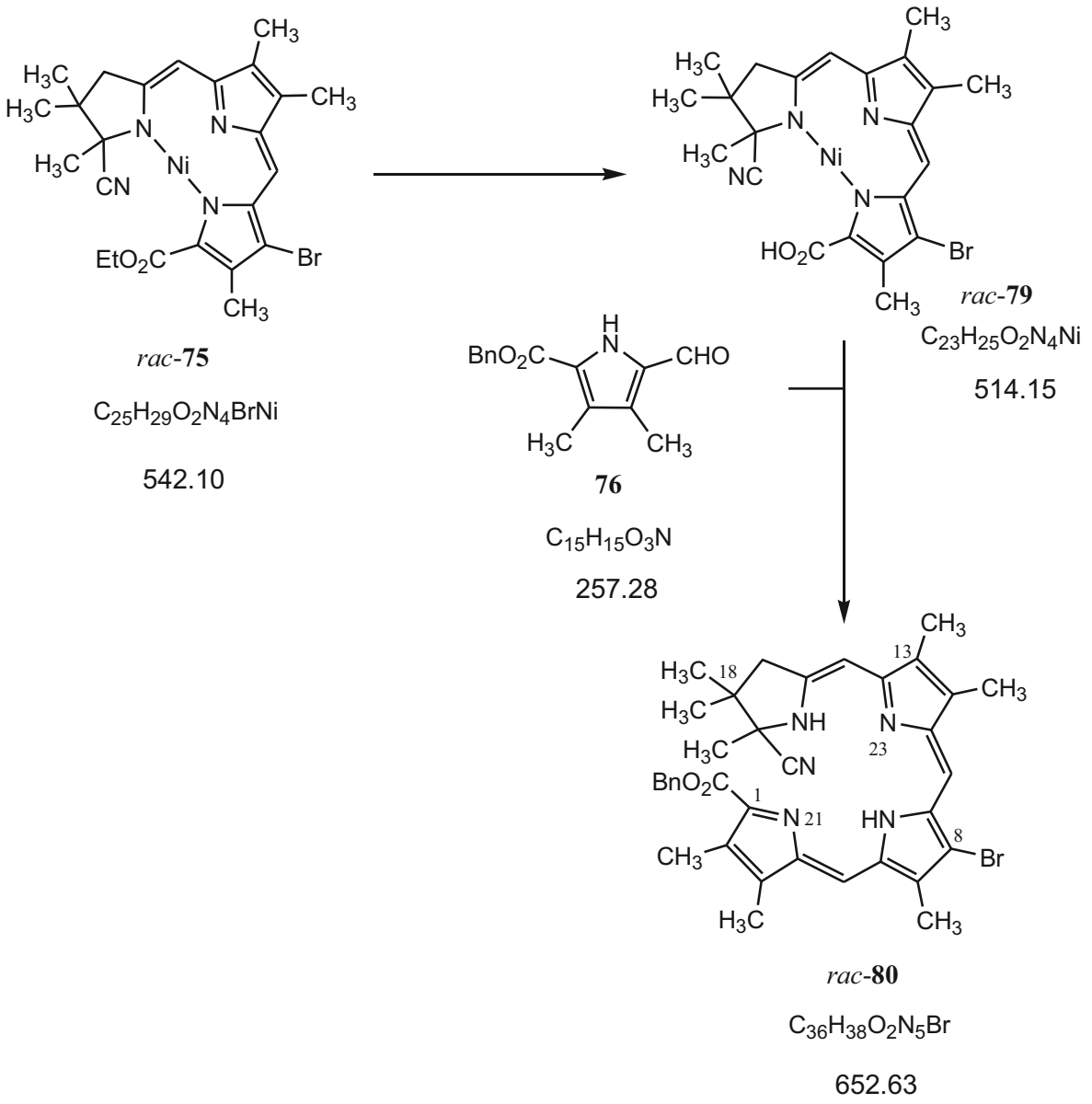
UV/ VIS (CH_2Cl_2): λ_{max} (ε) = 530 (26086), 490 (13056), 345 (18258), 298 nm (3910 cm^2mmol^{-1});

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.21 (s, 3H, 2a-C**H**$_3$), 1.28 (s, 3H, 2b-C**H**$_3$), 1.44 (t, 3H, -CH2-C**H**3), 1.76 (s, 3H, 1-C**H**$_3$), 2.06 (s, 3H, 7-C**H**$_3$), 2.20 (8-CH_3), 2.30 (s, 3H, 13-C**H**$_3$), 2.69/2.85 (AB-system, 2H, 3-C**H**$_2$), 4.62/4.67 (m, 2H, 14-CH_2C**H**$_3$), 5.55 (s, 1H, 5-C**H**), 6.57 (s, 1H, 10-C**H**);

MS (EI, 70 eV, direct, T = 200 °C): m/z (% rel. intensity) = 542 (10) $[M]^+$, 462 (100) $[M-Br]^+$, 407 (12) $[M-Br-HCN-C_2H_4]^+$, 389 (8) $[M–Br-CO_2C_2H_5]^+$, 363(5), 217(8), 204 (10);

HR-MS [EI, $C_{24}H_{27}O_2N_4BrNi$, R ≈ 10000]: Calculated: 540.06708;
Measured: 540.06765.

5.5.8 Synthesis of benzyl-(19*RS*)-8-bromo-19-cycano-17,18,19,21-tetrahydro-2,3,7,12,13,18,18,19-octamethyl-22*H*-bilin-1-carboxylate (80)



To a solution of nickel complex *rac*-**75** (5 mg, 9.2 µmol) in 3 mL of THF* was added a solution of 5 N KOH in MeOH / H_2O (9:1) (2 mL). The mixture was heated to 70 °C for 30 min.. After cooling, the mixture was transferred to the separating funnel, added with 10 mL of water and exhaustively extracted with 10 mL portions of CH_2Cl_2. The combined organic phases were filtered through a plug of cotton, concentrated by a rotary evaporator, and dried on a oil pump to afford the crude intermediate *rac*-**79**. A round bottomed flask with the crude carboxylic acid *rac*-**79**, equipped with a septum cap and a magnetic stirrer was evacuated under high vacuum and then gassed with argon. A solution of formyl-pyrrole-bezylcarbonate **76** (3.5 mg, 13.8 µmol, 1.5 eq.) in 2 mL of $CHCl_3$ and a solution of 0.4 N p-TsOH in $CHCl_3$*

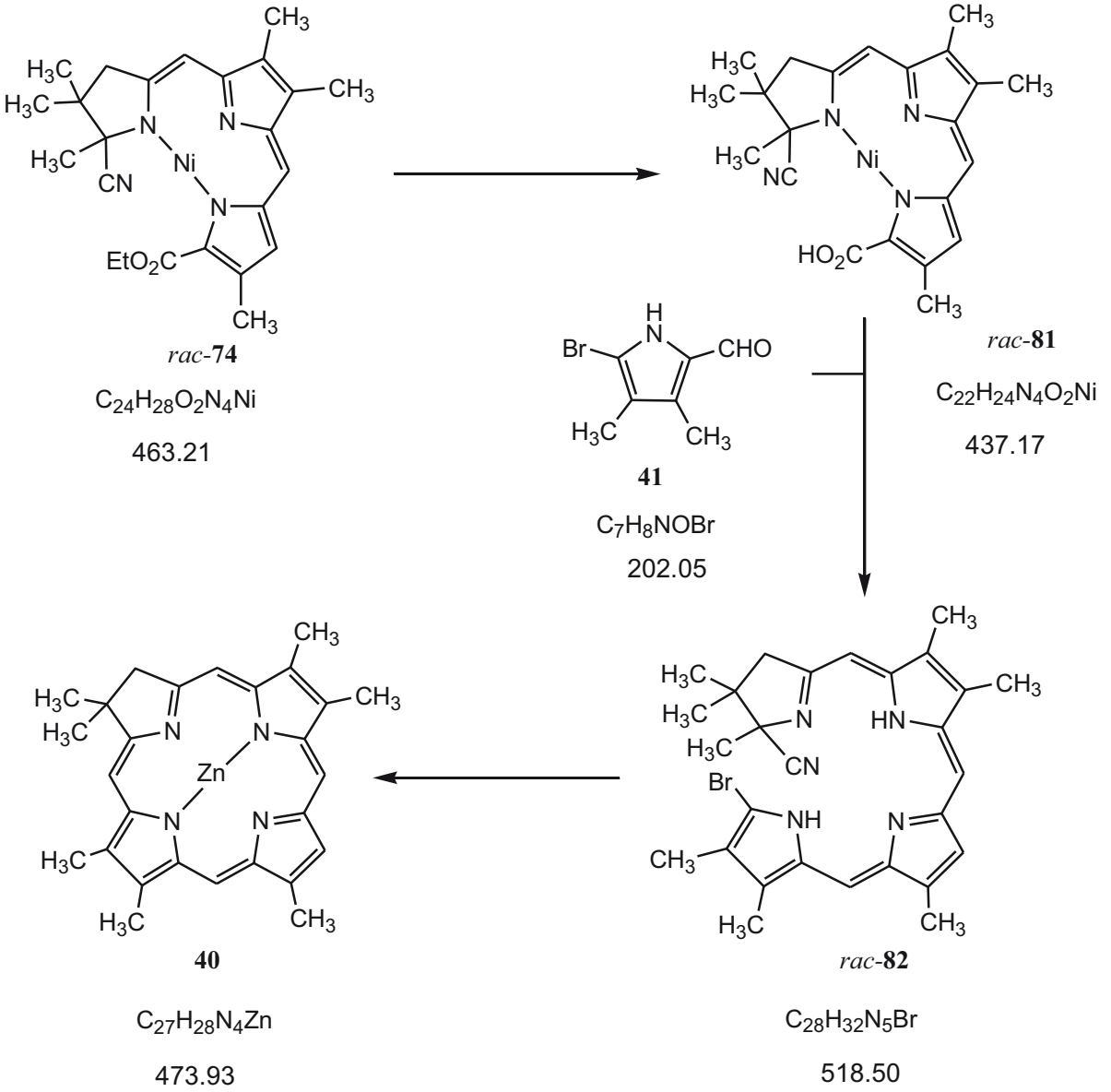
(0.3 mL) were then injected through the septum cap. The reaction mixture was stirred at rt. for 5 hours. After treating with 10 mL of sat. aq. $NaHCO_3$ solution, the mixture was extracted with 10 mL of CH_2Cl_2. The organic phase was filtered through a plug of cotton and concentrated by a rotary evaporator. The residue was purified by column chromatography (1 cm column, 10 g aluminum oxide, CH_2Cl_2) to yield a blue solid.

R_f : 0.6 (aluminium oxide, CH_2Cl_2/ PE 2:1);

MS (ESI, positive, MeOH): 652 $[M,^{79}Br + H]^+$, 654 $[M,^{81}Br + H]^+$, 674 $[M,^{79}Br + Na]^+$, 676 $[M,^{81}Br + H]^+$;

(ESI, negative, MeOH): 650 $[M,^{79}Br - H]^-$, 652 $[M,^{81}Br - H]^-$.

5.5.9 Synthesis of 2,3-dihydro-2,2,7,8,13,17,18-heptamethyl-22*H*,24*H*-porphinato]-zinc-(II) (40)



To a solution of nickel complex *rac*-**74** (6 mg, 0.012 mmol) in 3mL of THF* was added a solution of 5 N KOH in (MeOH/H_2O) (0.4 mL, 2mmol). The reaction mixture was heated to 70 ^oC for 45 min.. After cooling, the solution was treated with 10 mL of sat. aq. $NaHCO_3$ then extracted twice with 10 mL portions of CH_2Cl_2, the combined organic layers were filtered through a plug of cotton, concentrated and dried over oil pump to afford the crude free acid nickelcomplex *rac*-**81**. To a solution of crude acid product *rac*-**81** (5.2 mg, 0.0119 mmol) was added a solution of 5-bromo-3,4-dimethyldopyrrole-1-carbadehyde **41** (3.8 mg, 0.019 mmol, 1.5 eq.) and a solution of 0.4 N *p*-toluenesulfonic acid (0.4 mL, 0.16 mmol) in $CHCl_3$*. The

reaction mixture was stirred for 2.5 hours at rt.. The solution was then treated with 10 mL of sat. aq. $NaHCO_3$ solution, extracted 3 times with 5 mL portions of CH_2Cl_2. The organic phase was filtered through a plug of cotton and concentrated under reduced pressure. The resulting solid was purified by chromatography (10 g of neutral Al_2O_3, CH_2Cl_2) to afford tetracycle **82** (4.5 mg, 67 %) as a blue-green solid. To a solution of tetracycle *rac*-**82** (4.5 mg, 8.6 µmol) and $Zn(CH_3COO)_2$ 9.8 mg (0.052 mmol, 4.3 eq.) in 3mL of sulfolane was added 0.8mL of DBU. The reaction mixture was heated to 80 ^oC for 3 hours. After cooling, the solution was treated with 10 mL of sat. aq. $NaHCO_3$ then extracted 3 times with 5 mL portions of CH_2Cl_2. The organic extract was concentrated using a kugelrohr at 110 ^oC. The residue was purified upon column chromatography (10 g of silical gel, CH_2Cl_2) to afford chlorin **40** (2.8 mg, 49.2 %) as a green solid.

R_f: 0.6 (silica gel, PE/acetone 3:1);

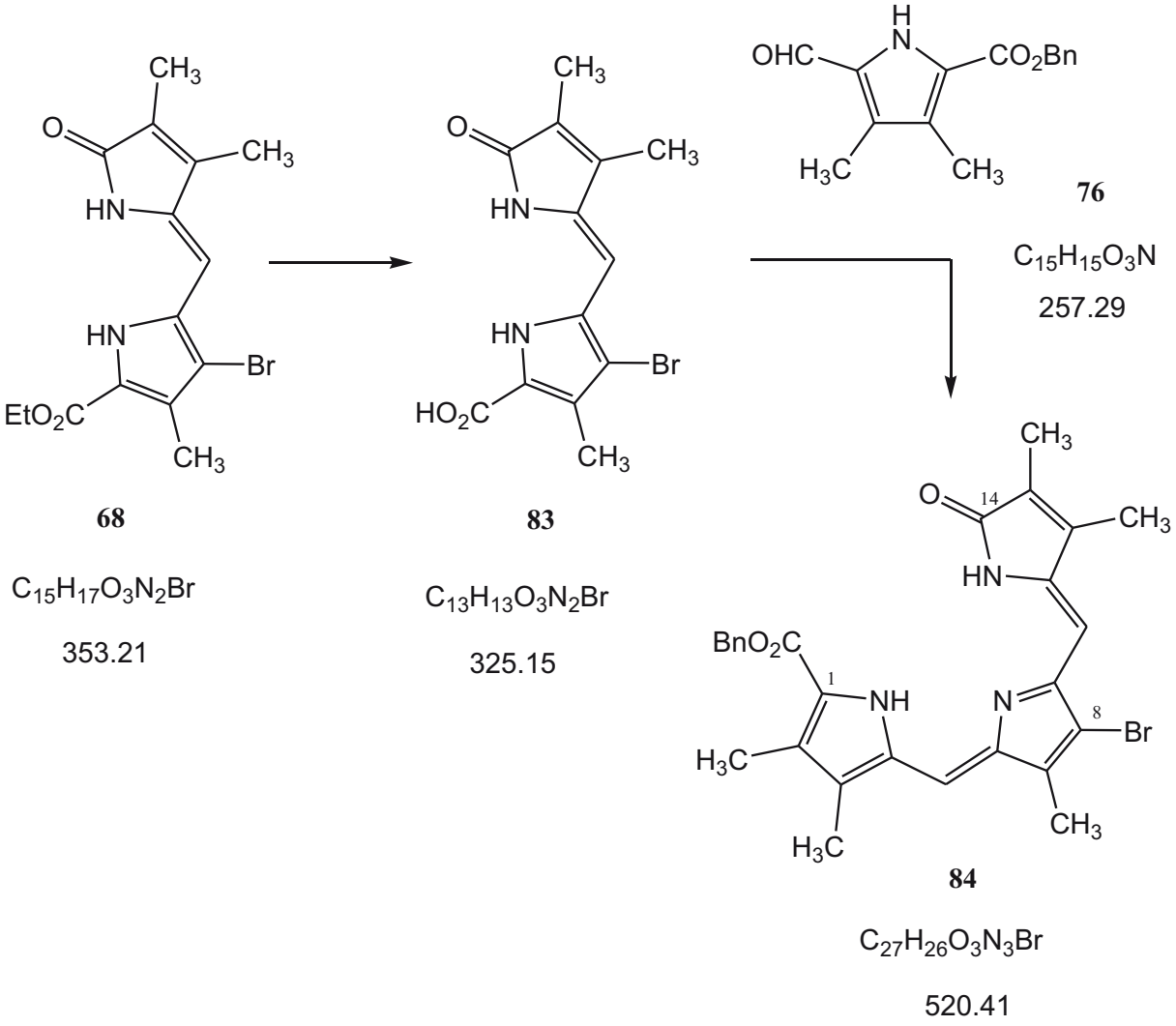
IR (KBr): $\tilde{\nu}$ = 2956 (w, CH_3), 2928 (m, CH_3), 2847 (w, CH_3), 1614 (m, C=C), 1485 (m), 1376 (m), 1233 (w), 1458 (w), 1132 (w), 1036 (w), 946 (w), 849 (w), 813 (w), 723 cm^{-1} (m);

UV/ VIS (acetone): λ_{max} (ε) = 610 (16038), 395 nm (80365cm^2mmol^{-1});

^{1}H NMR (360 MHz, C_6D_6): δ= ^{1}H NMR (360 MHz, C_6D_6) δ= 2.01 ppm (s, 6H, 2*2-C**H**$_3$), 3.23, 3.28, 3.33, 3.37, 3.49 (5*s, 10H, 7-, 18-, 8-, 17-,13- C**H**$_3$), 4.49 (s, 2H, 2-C**H**$_2$), 8.49 (s, 1H, 20-C**H**), 8.58 (s, 1H, 5 C**H**), 8.6 (12-C**H**), 9.38 (s, 1H, 10-C**H**), 9.51 ppm (s, 1H, 15-C**H**);

MS (ESI, positive, MeOH): 597 $[M-H]^-$, 629 $[M+CH_3O^-]$.

5.5.10 Synthesis of benzyl-8-bromo-15-hydro-14-oxo-2,3,7,12,13-pentamethyl-16*H*-tripyrrin-1-carboxylate (84)



To a solution of lactam **69** (22 mg, 0.062 mmol) in 6 mL of THF was added a solution of 5 N KOH in MeOH/H_2O (9:1) (0.8 mL, 1 mmol, 16 eq.). The mixture was stirred to 70 ^oC for 1 hour. After cooling, the reaction mixture was treated with 0.3 mL of TFA until the pH of the mixture was less than 7. The solvent was removed under reduced pressure and the solid was dried overnight to yield the crude acid **83**.

The crude acid **83** and 23.92 mg (0.093 mmol, 1.5 eq.) pyrrole **76** were dissolved in 10 mL of ($CHCl_3$/TEA 5:1). The mixture was connected to a sohlet apparatus and refluxed for 2 hours. After cooling, 5 mL of sat. aq. $NaHCO_3$ solution was then added to the mixture and the organic phase was separated. The aqueous phase was extracted twice with 10 mL portions of CH_2Cl_2. The combined extracts were dried through a plug of cotton and concentrated by a

rotary evaporator. The crude product was purified by column chromatography (10 g of Al_2O_3, CH_2Cl_2) and recristallized from $CHCl_3$ to give tripyrrin **84** (6.7 mg, 19 %) as red crystals.

Mp: 215 ^oC ($CHCl_3$);

R_f: 0.7 (silica gel, CH_2Cl_2);

IR (KBr): $\tilde{\nu}$ = 2923 (w, CH_3), 2854 (w, CH_3, CH_2), 1683 (C=O, benzyl ester), 1654 (s), 1464 (s), 1391 (m), 1370 (m), 1263 (s), 1205 (m), 1161 (m), 1105 (m), 938 (m), 911 (m), 856 (w), 83 (m), 774 (m), 753 (m), 696 (s), 627 (m), 506 cm^{-1} (m);

NMR (360 MHz, C_6D_6): δ = 1.58, 1.60 (s, s, 6H, 2-CH_3, 3-CH_3), 1.72, 1.83 (s, s, 6H, 12-C**H**$_3$, 13-C**H**$_3$), 2.23 (s, 8-C**H**$_3$), 5.74 (s, 2H, C**H**$_2$-benzyl), 6.00, 6.46 (s, s, 5-C**H**, 10-C**H**); 7.02 (m, 5H, C_6**H**$_5$-benzyl);

UV/ VIS (CH_2Cl_2): λ_{max} (ε) = 540 (24750), 320 (39600 cm^2mmol^{-1});

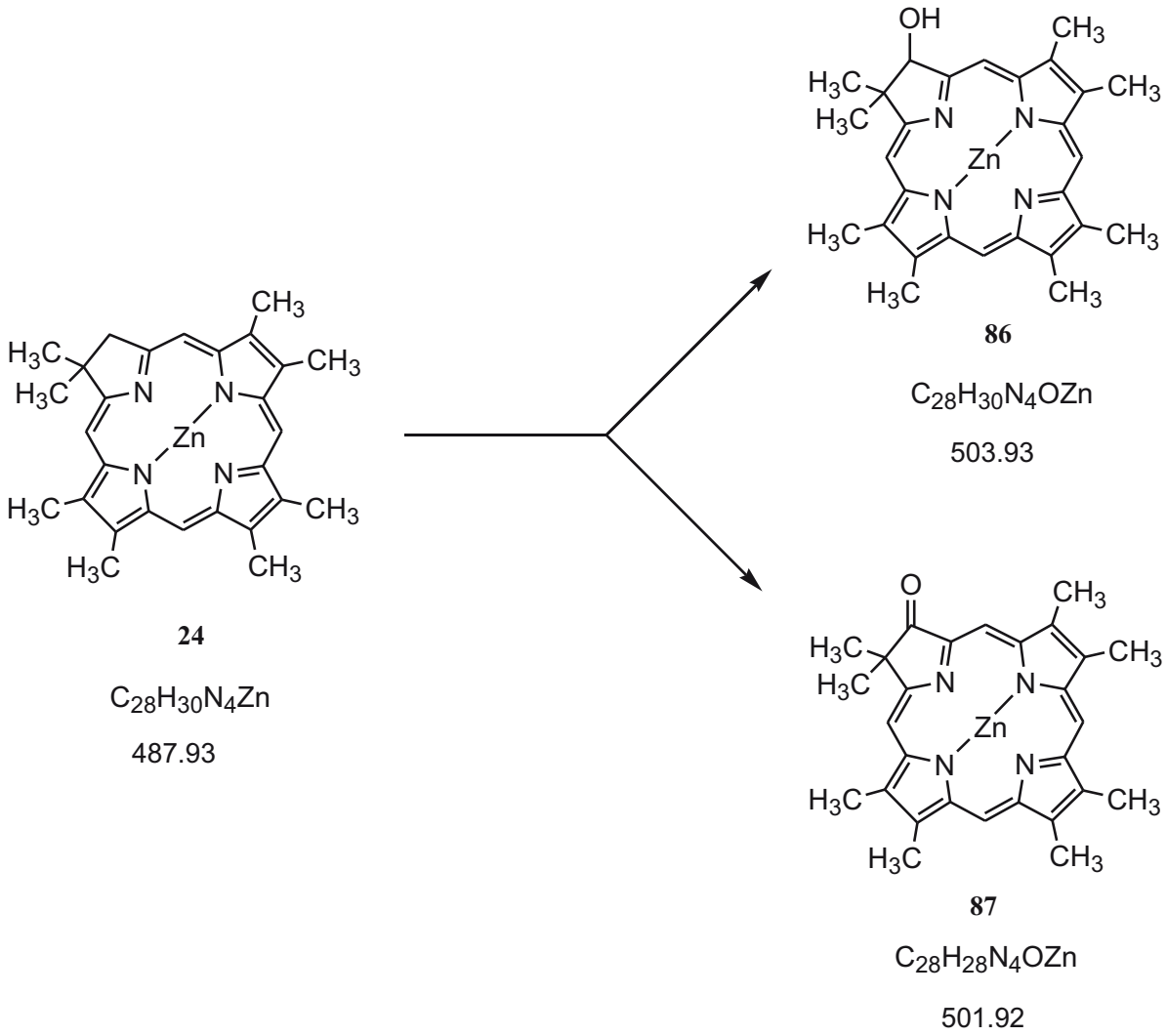
MS (ESI, positive, MeOH): 542 $[M,^{79}Br + Na]^+$, 544 $[M,^{81}Br + H]^+$, 558 $[M,^{79}Br + K]^+$, 560 $[M,^{81}Br + H]^+$;

(ESI, negative, MeOH): 518 $[M,^{79}Br - H]^-$, 520 $[M,^{81}Br - H]^-$;

HR-MS [MALDI, $C_{27}H_{26}O_3N_3Br$, R≈10000]: Calculated: 519.1157;

Measured: 519.1148.

5.5.11 Synthesis of [2,3-dihydro-3-hydroxyl- -2,2,7,8,12,13,17,18-octamethyl-22*H*,24*H*-porphinato]-zinc(II) (86) and [2,3-dihydro-2,2,7,8,12,13,17,18-octamethyl-3-oxo-22*H*,24*H*-porphinato]-zinc(II) (87)



24

$C_{28}H_{30}N_4Zn$

487.93

86

$C_{28}H_{30}N_4OZn$

503.93

87

$C_{28}H_{28}N_4OZn$

501.92

To a solution of chlorin **24** (6.2 mg, 0.012 mmol) in 4 mL of THF* cooled to -78 ^oC was added a solution of NBS (2.3 mg, 0.013 mmol, 1 eq.) in 1 mL of THF* through the septum cap under argon atmosphere. The reaction mixture was stirred at -78 ^oC for 2 hours then the cooling bath was removed. The reaction mixture was then warmed up to rt. and stirred for further 1 hour. 20 mL of dichlomethane was then added to diluted the solution and the reaction was quenched by addition of 30 mL of sat. aq. $NaHCO_3$ solution. The mixture was separated and the aqueous phase was extracted twice with 20 mL portions of dichlomethene. The combined organic phases were dried through a plug of cotton and concentrated under reduced pressure. The residue was purified by column chromatoghraphy (10 g of silica gel, PE/methyaceate 3:1) to afford hydroxylchlorin **86** (2.5 mg, 39 %) and oxochlorin **87** (1.2 mg, 18.8 %).

Characterization of hydroxylchlorin (86):

R_f: 0.3 (silica gel, PE/methylacetate 3:1);

IR (KBr): $\tilde{\nu}$ = 3436 (w, br.), 2924 (m, CH_3), 2854 (w, CH_3), 1625 (m), 1459 (m), 1139 (m); 867 cm^{-1} (m);

NMR (360 MHz, $CDCl_3$): δ = 1.93, 1.94 ppm (6H, 2 2-C**H**$_3$), 3.29 (6H, s, shouder, 2 C**H**$_3$, 3.33 (s, C**H**$_3$), 3.34 (s, C**H**$_3$), 3.36 (s, shouder, 2 C**H**$_3$), 6.07 (d, ^{3}J=5.9 Hz, 1H, 3-C**H**), 8.55, 8.80 (s, s, 2H, 5-C**H** and 20-C**H**), 9.47, 9.51 (s, s, 2H, 10-C**H** and 15-C**H**);

UV/ VIS (CH_2Cl_2): λ_{max} (ε) = 620(49260), 570(11330), 415(17232), 330(19704) nm (38198 cm^2mmol^{-1});

HR-MS [EI, $C_{28}H_{30}N_4OZn$, R ≈ 10000]: Calculated: 506.1668;
Measured: 506.1670.

Characterization of oxochlorin (87):

R_f: 0.6 (silica gel, PE/methylacetate 3:1);

IR (KBr): $\tilde{\nu}$ = 3468 (w, br.), 2960 (w, CH_3), 2923 (m, CH_3), 2854 (w, CH_3), 1709 (s, C=O), 1538 (w), 1463 (m), 1378 (w), 1261 (m), 1221 (w), 1147 (m), 1097 (m), 1023 (m), 802 cm^{-1} (m);

NMR (200 MHz, $CDCl_3$): δ = 2.09 ppm (6H, 2 2-C**H**$_3$), 3.26 (s, 3H, C**H**$_3$), 3.27 (s, 3H, C**H**$_3$), 3.36 (s, 3H, C**H**$_3$), 3.37(s, 3H, C**H**$_3$), 3.41(s, 6H, 2 C**H**$_3$), 8.9, 9.4 (s, s, 2H, 5-C**H** and 20-C**H**), 9.45, 9.59 (s, s, 2H, 10-C**H** and 15-C**H**);

UV/ VIS (CH_2Cl_2): λ_{max} (ε) = 610(10899), 395(53133) nm (38198 cm^2mmol^{-1});

HR-MS [EI, $C_{28}H_{28}N_4OZn$, R ≈ 0000]: Calculated: 500.1554;
Measured: 500.1554.

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