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Treball Final de Grau

Supramolecular aggregates of sulfonated derivatives of tetraphenylporphyrin as tentative asymmetric counteranions in organocatalysis.
Agregats supramoleculars de derivats sulfonats de la tetrafenilporfirina com a possibles contraanions asimètrics en organocatàlisi.

Bernat Soler Guix

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Universitat de Barcelona

B:KC Barcelona Knowledge Campus
Campus d'Excel·lència Internacional

Sorprendre'ns per quelcom és el primer pas de la ment cap al descobriment.

Louis Pasteur

Aquest treball ha estat supervisat pel Dr. Joaquim Crusats a qui vull agrair enormement la seva dedicació, paciència i bon humor.

També vull agrair especialment al Dr. Albert Moyano pels seus consells que han orientat també la línia d'investigació del treball.

I d'altra banda agrair al Dr. Zoubir El-Hachemi i a l'Aitor Arlegui per la seva ajuda en el decurs de la realització del treball sempre que els he necessitat.

REPORT

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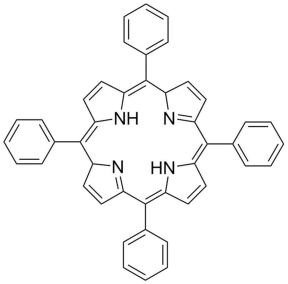

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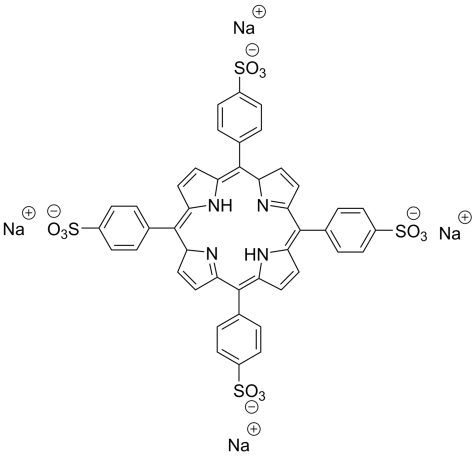

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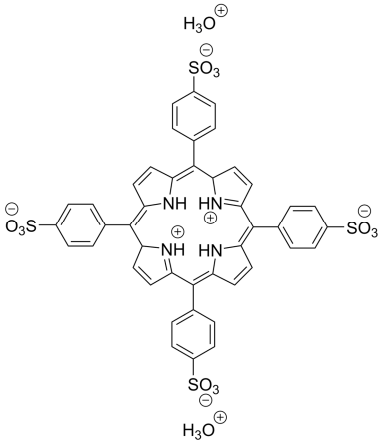

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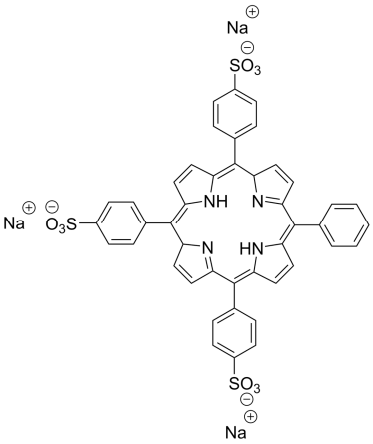

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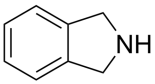

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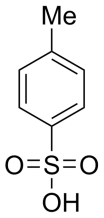

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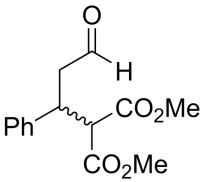

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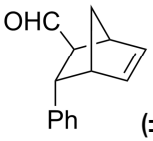

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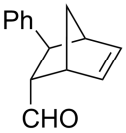

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1. SUMMARY

On this research project it has been studied the viability of using supramoleculary chiral aggregates of sulfonated self-assembling porphyrins as chiral counter anions on Michael and Diels-Alder organocatalytic reactions on water, which proceed through a cationic reaction intermediate to determinate the feasibility of using a ACDC (Assymetric counteranion directed catalysis) strategy to transfer the supramolecular chirality of the aggregates on an organic reaction product enantiomeric excess.

To do so, a method to prepare the chiral aggregates of the *meso*-5,10,15,20-tetrakis(4-sulfonatofenil)porphyrin on its zwitterionic form has been optimized in order to prevent the presence of other counter anions which could also interact with the cationic intermediates from the organocatalytic reactions. It has been proved that the zwitterionic porphyrin not only maintains the aggregation state of the sodium salt, also, the supramolecular chirality still remains even though the addition of the basic organocatalistys (pyrrolidine and isoindoline). Finally it has been shown for the studied Michael and Diels-Alder reactions, exists a narrow window of experimental conditions where it is possible to use this catalysts under ACDC conditions.

Keywords: porphyrin, supramolecular aggregates, self-assembly, chirality, organocatalysis, ACDC

2. RESUM

En aquest treball d'investigació s'ha estudiat la viabilitat d'utilitzar agregats supramoleculars quirals de porfirines sulfonades auto-ensamblants com a contra anions quirals en reaccions de Michael i de Diels-Alder organocatalitiques en aigua que concorren a traves d'un intermedi de reacció catiònic, amb la finalitat de poder establir si es factible utilitzar una estratègia ACDC (Assymetric counteranion directed catalysis) per transferir la quiralitat dels agregats supramoleculars cap a un excés enantiomèric del producte d'una reacció orgànica.

Per fer-ho s'ha optimitzat un mètode per preparar agregats quirals de la *meso*-5,10,15,20-tetrakis(4-sulfonatofenil)porfirina en forma zwitterionica per evitar la presencia d'altres contra anions que podrien també interaccionar amb els intermedis catiònics de les reaccions organocatalítiques. S'ha comprovat que la porfirina zwitteriònica preparada no només manté l'agregació que presenta la sal sòdica, sinó també la quiralitat supramolecular tot i l'addició dels organocatalitzadors bàsics (pirrolidina i isoindolina). Finalment, s'ha demostrat que per les reaccions de Michael i Diels-Alder estudiades existeix un estret marge de condicions experimentals en les quals és possible utilitzar aquests catalitzadors en condicions ACDC.

Paraules clau: porfirina, agregats supramoleculars, auto-ensamblatge, quiralitat organocatàlisi, ACDC

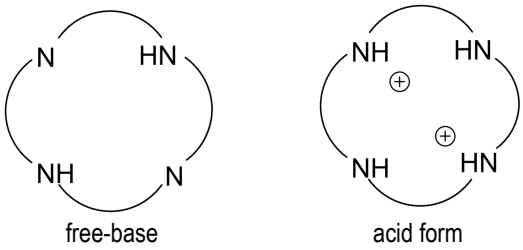
3. INTRODUCTION

Porphyrins and catalysis will be the central points of this final grade project; more precisely, the sulfonated tetraphenyl porphyrins and organocatalysis.

Tetraphenyl porphyrins are easily synthetized by condensing pyrrole and benzaldehyde. They are non-polar macrocycles, however, porphyrins treated with sulfuric acid are water-soluble because of the sulfonated groups attached to the ring. This is the reason why sulfonated porphyrins are so interesting.

3.1. SUPRAMOLECULAR AGGREGATES

The porphyrin macrocycle has two basic pyrroleninic nitrogen atoms in the central part of the macrocycle which can be protonated in acidic media (Scheme 1).

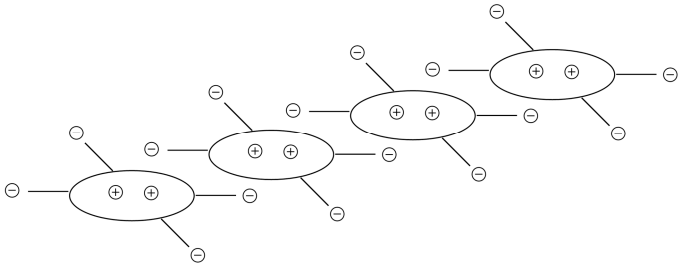


Scheme 1. Schematic representation of the porphyris core.

Sulfonated tetraphenyl porphyrins have a range of pH values in which the macrocycle is completely protonated while the sulfonate groups are still deprotonated. Working between these pH values the formation of porphyrin aggregates has been detected.[1] This process is known as homoassociation when all the porphyrin units in the aggregate are equal. In the aggregation process hydrophobic, ionic and hydrogen bonding interactions are the main forces involved in the self-assembly of porphyrin molecules to build the aggregate.

The fundamental structure of the aggregate consists of a stacking of porphyrins in which two sulfonate groups from neighbour porphyrins units interact with the positively charged porphyrin

centre forming the J-aggregates (scheme 2). This type of compounds are called self-assembling porphyrins.



Scheme 2. Mono-dimensional J-Aggregate structure of the $TPPS_4$ (edge-to-edge).

There are two types of aggregation structures: the J-aggregates (edge-to-edge interaction of the chromophores) and the H-aggregates (face-to-face interaction of the chromophores), depending on the growth tendency; the J-aggregates are based on the mono-dimensional placement of molecules and the H-aggregates originate from the two-dimensional combination of J-aggregates.

Also the mesoscopic structure of the 3D aggregate growth has been studied[2].

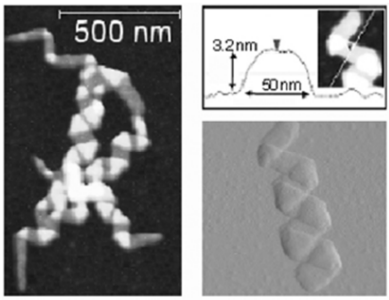


Figure 1. $TPPS_3$ aggregate AFM images coming from solutions (3 μM porphyrin, 0.34 M NaCl, H_2SO_4 pH = 1.7) prepared by rotary evaporation. (from ref. [2]).

The $TPPS_3$ aggregates fold in ribbon shaped 3D structures (Figure 1).

An outstanding fact about these porphyrins is that although the basic unit on the aggregate structure, each sulfonated tetraphenyl porphyrin molecule, is achiral. The aggregation presents a spontaneous symmetry breaking process, as it can be observed by circular dichroism[3] (Figure 2).

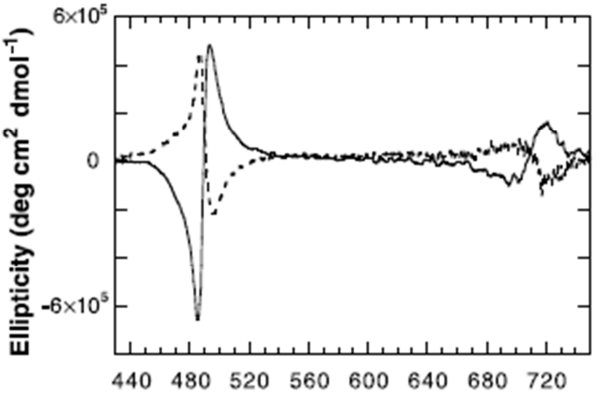


Figure 2. CD spectra of two solutions (3 mM) of homoassociates of $TPPS_3$ corresponding to two characteristic experiments of vortex direction during the rotary evaporation (from ref.[3]).

It is interesting that this supramolecular chirality can be controlled at will by the direction of macroscopic vortical stirring by slowly concentrating an acidic $TPPS_3$ solution[3].

3.2. ORGANOCATALYSIS

The term organocatalysis describes the acceleration of chemical reactions through the addition of an organic compound. The interest in this field has increased in the last few years because of its efficiency and selectivity of many organocatalytic paths for established organic reactions. Organocatalysis is becoming a very usefull tool in the construction of complex molecules[4].

A big challenge in organic synthesis is the stereoselectivity of the reactions leading to the desired product, as most reactions do not proceed in a stereoselective way. To solve this problem there is the asymmetric catalysis, a type of catalysis in which a chiral catalyst directs the formation of a chiral compound such that formation of one particular stereoisomer is favored, and potentially improving efficiency and avoiding waste.

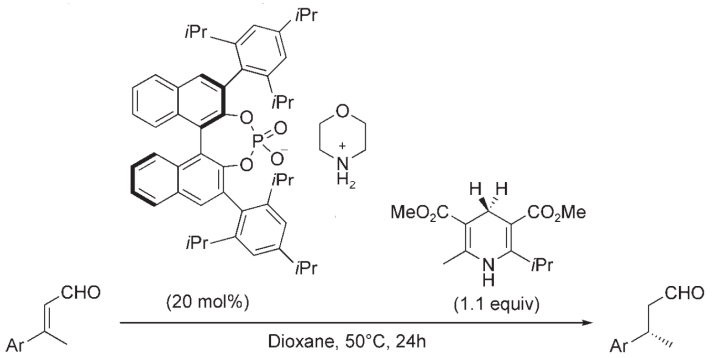
Asymmetric catalysis can be done by using all types of chemical interactions between substrates and catalysts, including covalent bonding (enamine catalysis for example) and different types of noncovalent interactions, such as hydrogen bonding or ion pairing[5].

In this study we will focus on the ion pairing chemical interaction between the reaction intermediate and a chiral ion. The underlying idea is that some cationic intermediates are

necessarily accompanied by a counter anion and, if this anion is chiral and a sufficient association can be achieved, reactions can proceed enantioselectively. This strategy is called asymmetric counter-anion directed catalysis (from now on ACDC).

In other words, this strategy refers to the induction of enantioselectivity in a reaction proceeding through an ionic intermediate by means of ion pairing with a chiral anion provided by the catalyst.

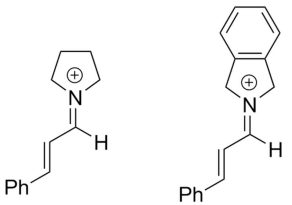
This method has been successfully tested, for example[6].



Scheme 3. Schematic summary of a stereoselective hydrogenation reaction carried out with the ACDC method (from ref.[6]).

In the reaction depicted on scheme X, the huge binaphthol-derived phosphate salt (TRIP), is used as a chiral counteranion for an iminic intermediate of a hydrogenation reaction that gets attached to the favored side of the intermediate letting the reaction proceed with a high stereoselectivity.

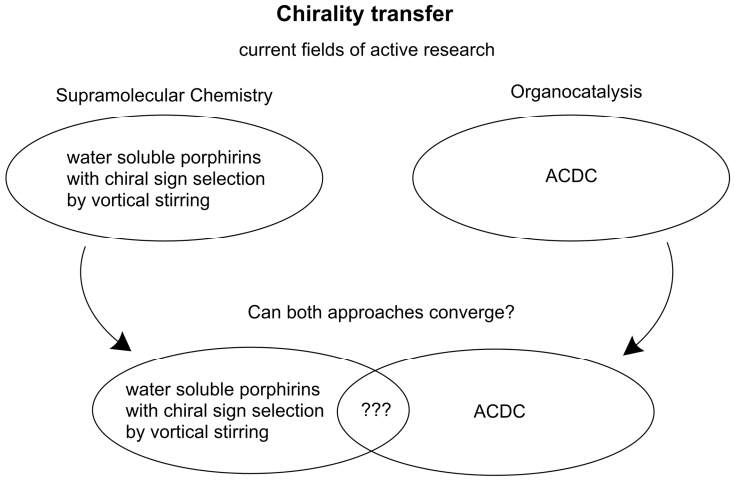
Michael and Diels-Alder reactions are two good candidates to proceed under ACDC organocatalytic conditions due to presence of an iminic intermediate (Scheme 4).



Scheme 4. Cationic intermediates of a Michael and Diels Alder reactions using cinnamaldehyde as a reactive, left, pyrrolidine as organocatalyst, right isoindoline.

3.3. A yet unexplored area

It is nowadays well established that there is the possibility of transferring the chirality of macroscopic stirring forces to the supramolecular chirality of a porphyrin aggregate and also to transfer the chirality of anions into enantiomeric excesses of the products of organic reactions. However, no one has ever achieved to transfer the macroscopic chirality of vortical stirring to the configurational ratio of an asymmetric carbon atom.



Scheme 5. Schematic representation of the goal of this work.

These two different study fields have very different optimized experimental conditions and, *a priori*, it is not immediate to make both approaches compatible. In order to do so, this study will assess the feasibility or not of finding a set of experimental conditions under which both approaches to chirality transfer can coexist (scheme 5). This could open new avenues for the transfer of the macroscopic chirality of stirring to an enantiomeric excess of a chemical reaction.

4. OBJECTIVES

The primary objective of this project is to assess the feasibility or not of finding a set of experimental conditions under which two different well-established research fields can converge: (1) the transfer of the chirality of a macroscopic vortical stirring force into the supramolecular chirality of a water-soluble porphyrin aggregate, and (2) using these chiral porphyrin homoassociates to transfer the chirality to a disymmetric molecule using a strategy based on asymmetric counter-anion directed catalysis (ACDC).

In order to achieve this goal, the following subobjectives are essential:

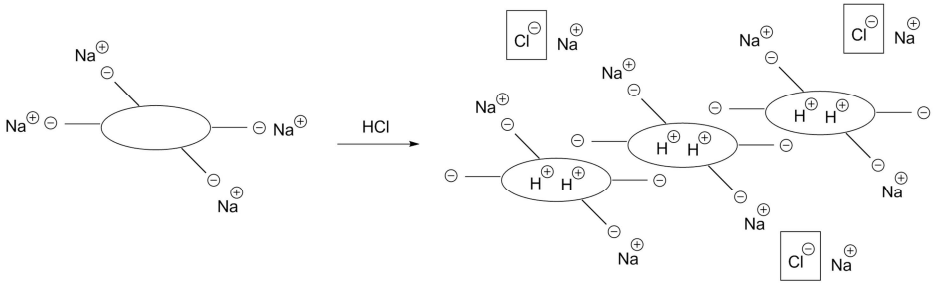
(1) To determine whether or not it is possible to prepare a supramolecularly chiral acidic porphyrin aggregate in water free of other anions whose structure is stable in the presence of the organocatalyst (ACDC compatible conditions).

(2) To set up some appropriate experimental conditions for organocatalytic reactions in water under which the supramolecular chirality of the porphyrin aggregates is preserved.

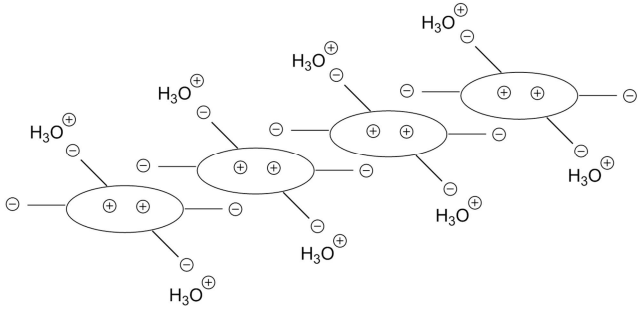
5. RESULTS AND DISCUSSION

Although the selection of the chiral sign emerging during the spontaneous symmetry breaking of water-soluble *meso*-4-sulfonatophentlporphyrins can only be controlled at will by the direction of macroscopic vortical stirring in the case of $TPPS_3$[3], here all the experiments will be performed with $TPPS_4$. The tetrasulfonated counterpart is much easier to obtain in large quantities avoiding tedious purification procedures[7] and it also spontaneously breaks chiral symmetry during its aggregation process, making it useful for the purpose of this exploratory investigation.

In order to assess the possibility of using a self-assembling sulfonated porphyrin as a supramolecular asymmetric counter anion for an iminic intermediate, using the ACDC strategy, the sodium $TPPS_4$ salt cannot be used (scheme 6). Note that the inner core of the porphyrin ring needs to be protonated at its pyrroleninic nitrogen atoms and the counteranions introduced during the acidification process would compete with the free lateral sulfonato groups of the aggregated porphyrin of the chiral supramolecular aggregate making the whole intended ACDC approach ineffective. To overcome this drawback, the zwitterionic tetrasulfonatoporphyrin is needed (zw-$TPPS_4$).



Scheme 6. Schematic representations of the sodium $TPPS_4$ acidification with HCl, squared the problematic chloride counteranion.

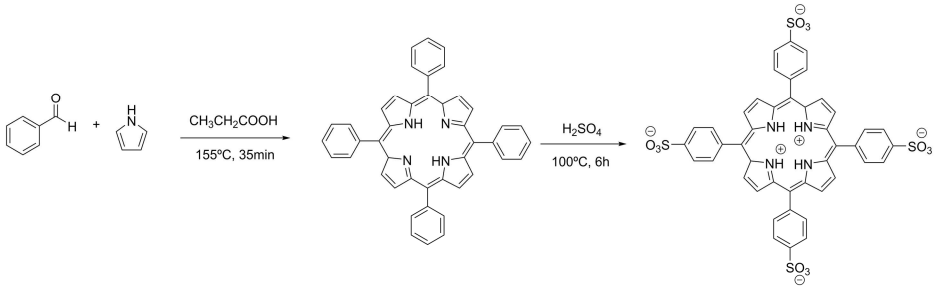


Scheme 7. zw-$TPPS_4$ aggregate structure scheme.

If the zw-$TPPS_4$ (Scheme 7) could be obtained in large quantities, and its supramolecular aggregates were stable when neutralized with two equivalents of the basic organocatalyst at an appropriate range of concentrations, then the ACDC approach might be successful. In what follows, the preliminary results of this approach are presented.

5.1. ZW-TPPS4 PREPARATION

The $TPPS_4$ was obtained by sulfonating the previously prepared TPP, which was done by the benzaldehyde and pyrrole condensation (Scheme 8). TPP purity was checked by UV-visible and TLC analysis. After recrystallization, the molar extinction coefficients matched closely to the described ones [7], the very small variations are caused by the presence of some chlorin[8] (See appendix 3).



Scheme 8. $TPPS_4$ total reaction scheme.

The zw-$TPPS_4$ can be prepared by obtaining at first the sodium salt of $TPPS_4$ and then replacing the sodium cations with hydronium ions using a cation-exchange resin. However, although this approach might be useful to obtain enough quantity of pure material to study the supramolecular part of the project, this would be useless if then larger quantities of the material were not conveniently available for synthetic procedures. Thus, a new method is studied for the zw-$TPPS_4$ preparation taking advantage of its ability to form precipitates in the acidic medium of the sulfonation reaction.

During the work-up of the synthetic procedure the reaction crude was washed with miliQ water several times and centrifuged to separate the sulfuric solution from the precipitate as supernatant waters, aiming to reach a point with the minimum amount of sulfuric acid in solution while the precipitate still remains.

During the viability study of the new zw-$TPPS_4$ preparation method, three different samples were obtained. The first sample revealed if the method is viable or not, and the subsequent ones allowed to optimize the synthetic preparation.

First sample. The precipitate obtained in the sulfonation process was subjected to a series of consecutive washings with water inside a centrifuge tube (see the Experimental Section). The pH measurement of the supernatant water is taken as a reference value to check the effectiveness of the washing progress.

Table **1**. Effect of stirring the sample on the dilution phase.

Entry	pH	Stirring
1	-0.77	No
2	-0.61	No
3	-0.33	No
4	0.08	No
5	-0.64	Yes
6	0.1	Yes
7	0.34	Yes
8	0.48	Yes
9[(a)]	0.28	Yes
10[(a)]	-0.01	Yes

[(a)]Done after a failed lyophilisation attempt.

The first time the sample was stirred (Entry 5) the pH decreased drastically, this means that more sulfuric has been released from the $TPPS_4$ precipitate, from now on every wash was vigorously stirred (Table 1).

A lyophilisation attempt was made after wash number 8 (entry 8), but it was not successful because a mud-like solid was obtained, the pH also after the lyophilisation, however, it helped to remove more sulfuric acid.

Table **2**. Effect of sonicating the sample on the dilution phase.

Entry	pH	Sonicated
8	0.48	No
9	0.28	No
10	-0.01	No
11	0.7	Yes
12	0.82	Yes
13	0.68	Yes

Sonicating the diluted sample does not have a relevant effect on the washing progress (Table 2).

After the 12th wash the sample was diluted on a larger water volume an divided on two tubes, after centrifuging, on one of the tubes the precipitate disappeared, pH measurement = 1.59, in the other still remained some solid, pH measurement = 1. In conclusion, the end of the washing process has to be before reaching a pH of the supernatant solution of 1.5.

After every wash, the quantity of sulfuric acid was tested also adding on a small fraction of the supernatant water few drops of a barium chloride solution. On the initial washes a white precipitate appeared clearly due to the formation of the barium sulfate salt and on the last washes the formation of a light green precipitate was observed corresponding to the formation of the barium salt of the $TPPS_4$ aggregates.

The lyophilisation process was repeated because of the mud-like precipitate formation on the first attempt, after wash (entry 8, Table 1), pH = 0.5, this means there was still too much sulfuric acid on the precipitate so it has to be washed more times. The last successfully lyophilisation attempt after wash entry 15, pH = 1, a green solid was obtained, this confirms the conclusion to stop the washing process at pH = 1 of the supernatant water.

Second sample. Another sample was obtained by recycling the $TPPS_4$, all the supernatant waters obtained on the previous process (first sample) were poured together on a big round bottom flask and the exceeding water was eliminated at the rotary evaporator.

Table **3**. Effect of introducing a wash with an HCl 0,1M solution.

Entry	pH
1	-0.98
2	-0.14
3	-0.1
4	0.56
5	1.02
6	0.7
7	0.9
8[a]	0.84
9	1.16
10	1.37

[a]HCl 0.1M solution wash.

The idea of washing with an HCl solution is aimed to replace the sulfate anions with the chloride anions then, because of the HCl volatility, it is removed on the lyophilisation phase by evaporation.

On the Second Sample method (Table 3) it seems that the $TPPS_4$ should have a higher quality (i.e. less content of residual acid), based on the pH measurements of the last wash, compared to the one prepared as first sample.

The quality comparison between samples will be explained later.

Third sample. Using the previous optimized method to obtain the zw-$TPPS_4$, another sample was prepared from a new TPP sulfonation reaction crude (Table 4).

Table **4**. Washing process.

Entry	pH	Entry	pH
1	-0.82	11[a]	0.52
2	-0.63	12	0.94
3	-0.02	13	0.94
4	0.21	14	0.45
5	0.33	15	0.71
6	0.21	16[b]	0.63
7	0.43	17[a]	0.71
8	0.52	18	0.8
9	0.72	19	0.99
10	0.89	20	1.17

[a]HCl 0,1M solution wash
[b]A solid was obtained after this wash by lyophilisation, 120% yield, sulfuric acid excess, it has to be washed again.

The different quality of the three samples will become clear when the neutralization of the zw-$TPPS_4$ samples with the secondary amines (organocatalysts) are presented. The relevant

fact, though, is that it is indeed possible to obtain large quantities (in the gram scale) of lyophilized zw-$TPPS_4$ for the purpose of this study.

5.2. SUPRAMOLECULAR CHEMISTRY OF ZW-$TPPS_4$

A first scope was done on the supramolecular and acid-base properties, followed using the UV-vis technique, of the zw-$TPPS_4$ aggregate as reference values for supporting afterwards experiments.

It is important to check the acid-base behaviour of our zw-$TPPS_4$ as it will be cohabitating with the basic amine organocatalyists in the crude reaction.

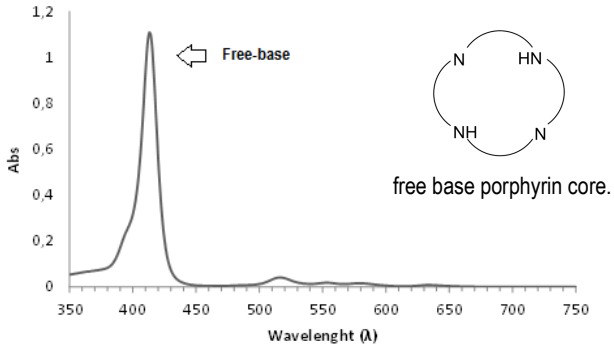


Figure 3. UV-vis spectra corresponding to a $TPPS_4$ solution ($3{,}1 \cdot 10^{-6}$M), neutralized with Na_2CO_3. Cell path 1cm.

For the basic form of the sulfonated *meso*-tetraphenyl porphyrins a 413nm band appears Figure 3).

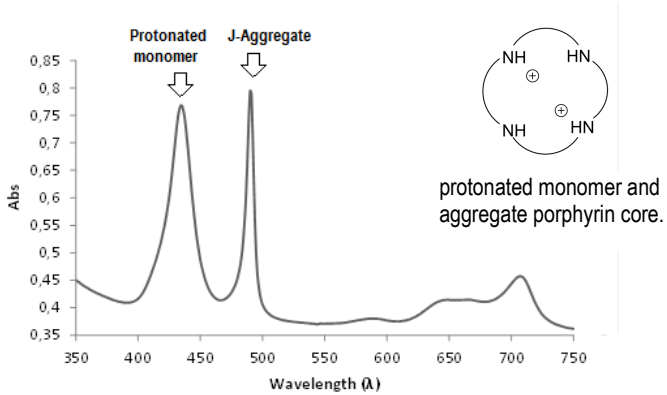


Figure 4. UV-vis spectra corresponding to a $TPPS_4$ solution ($8{,}15 \cdot 10^{-5}$M). Cell path 1cm.

The edge-to edge monodimensional J- aggregate has an absorption band at 490nm and at 433nm appears the band corresponding to the same protonated structure, but without aggregation (Figure 4).

For our approach exploration we want to aggregate structure to be the predominant anion in solution or the ACDC strategy will not take place, so the aggregate state is checked in function of the dilution effect, studied by UV-Visible spectrometry (Figure 5).

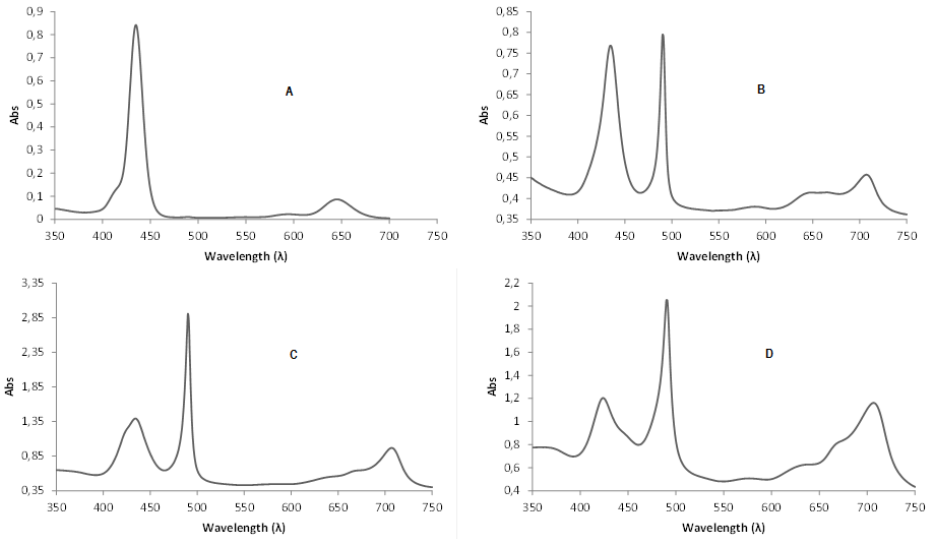


Figure 5. UV-visible spectra of different zw-$TPPS_4$ solutions in water: A, $3{,}66 \cdot 10^{-6}$ M, cell path 1cm; B, $8{,}15 \cdot 10^{-5}$ M cell path 1mm; C, $5 \cdot 10^{-4}$ M, cell path 1mm; D, $3{,}26 \cdot 10^{-3}$ M, cell path 0.1mm.

For solution A the zw-$TPPS_4$ is completely on its monomeric form (433 nm), the dilution is too high, at solution B with a higher concentration the absorption band corresponding to the aggregate (490 nm) is clearly present and for C and D the aggregate presence is clearly predominant. Consequently, to keep the aggregate state in the planned ACDC experiments they have to be done at high concentrations, 10^{-4} M or above.

zw-$TPPS_4$ is a strong organic acid due to the sulfonate groups it determines the pH medium, at the same time the pyrroleninic nitrogen atoms of the porphyrin core are protonated by this acid medium, favoring the assembling of the porphyrin molecules to generate the aggregates; therefore, zw-$TPPS_4$ controls itself aggregation state depending on its concentration.

The pH of the solutions can be influenced by their saturation with atmospheric CO_2; this would not only change the pH of the medium but it would also prevent the ACDC approach to be effective. To check if it was a relevant effect, a very diluted $TPPS_4$ solution was prepared and the UV-Visible spectra was recorded before and after applying a nitrogen stream during a few minutes, (see Appendix 1). The observed difference was very small and it could be concluded that this was only relevant at micromolar concentrations of the porphyrin.

It is known how the $TPPS_4$ aggregation takes place in water but not in methanol and it would be very interesting for future studies to expand this approach exploration to the organic solvent procedure. In this regard, the UV-Visible spectra was recorded for a $TPPS_4$ methanol solution before and after adding a salt excess to increase the ionic force and theoretically improve the aggregation simulating the $TPPS_4$ sodium salt (see Appendix 2). Interestingly, aggregation was observed in both cases, for the salt excess case there was a huge aggregation.

5.3. NEUTRALIZATION OF THE ZW-$TPPS_4$ AGGREGATES WITH THE ORGANOCATALYST

If the zw-$TPPS_4$ aggregates need to be used in the intended ACDC approach they have to be stable in the presence of two equivalents of the organic base used in catalysis. Note that larger amounts of base would neutralize the porphyrinic core and, hence, the free-base porphyrin would necessarily be in the achiral monomeric form. See the previous $TPPS_4$ acid-base explanation on supramolecular chemistry section.

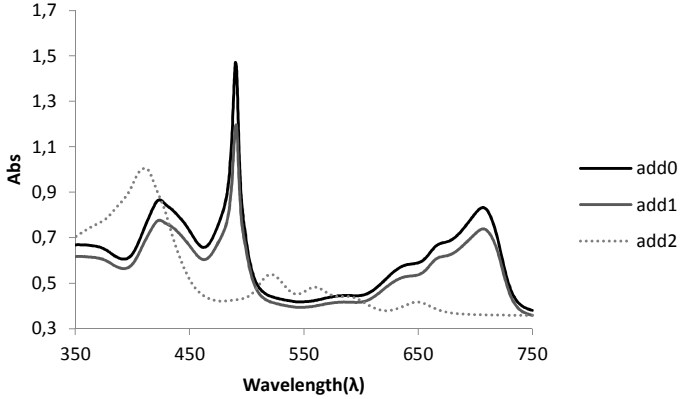


Figure 6**.** Uv-Vis spectra corresponding to a solution 2 ml of a $TPPS_4$ (second sample) (0,0036M, 0,007mmols) neutralized with pyrrolidine; each addition corresponds to 55µL from a 0,26M pyrrolidine solution (0,014mmols). "add0", "add1" and "add2" correspond to the initial $TPPS_4$ solution, and after the addition of 2 and 4 equivalents of base respectively. Cell path 0.1mm.

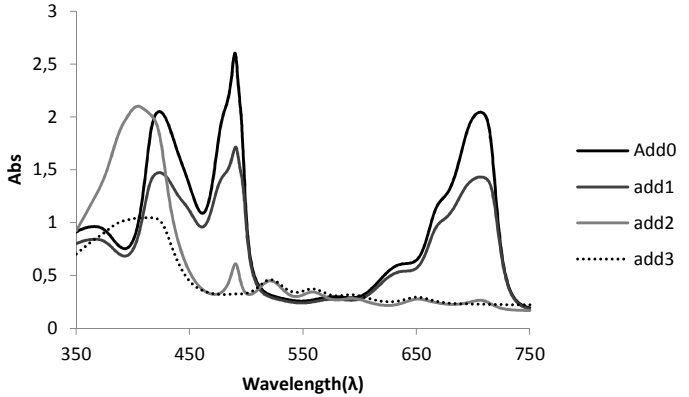


Figure 7**.** Uv-Vis spectra corresponding to a solution 2 ml of a $TPPS_4$ (Third Sample) solution (0,0045M, 0,009mmols) neutralized with isoindoline, each addition corresponds to 83µL from a 0,217M isoindoline solution (0,018mmol), "add0", "add1", "add2" and "add3" correspond to the initial $TPPS_4$ solution, after the addition of 2, 4 and 6 equivalents, 2 equivalents each time. Cell path 0,1mm.

The neutralization process UV-visible spectres reveal that the aggregation state of the zw-TPPS4 remains even the organocatalyst addition, with 2 equivalents in both cases (Figure 6 and Figure 7). On each addition the aggregate peak decreases until the complete neutralization depending on its "purity".

Table **5**. zw-$TPPS_4$ neutralization results.

Entry	zw-$TPPS_4$	Catalyst (base)	Base equiv.	pH (last wash)
1	first sample	pyrrolidine	8	1
2	first sample	pyrrolidine	6.5	1
3	second sample	pyrrolidine	4	1.34
4	third sample	pyrrolidine	6	1.17
5	third sample	isoindoline	6	1.17

The ideal molar equivalents of pyrrolidine/isoindoline for the complete neutralization of the $TPPS_4$, if all the sulfuric was removed in the preparation process, would be four. Note that this fits with one of the samples prepared using the HCl solution washing process and with the highest pH of the last wash (Table 5), so this method is really good to obtain the zw-$TPPS_4$ and, in principle, to use it in the intended ACDC approach.

Another essential requirement for the ACDC approach is that the zw-$TPPS_4$ in the presence of two equivalents of the organocatalytic base, not only must preserve the aggregation of the porphryrin but also the supramolecular chirality of the aggregates. This was confirmed with CD spectroscopy (Figure 8).

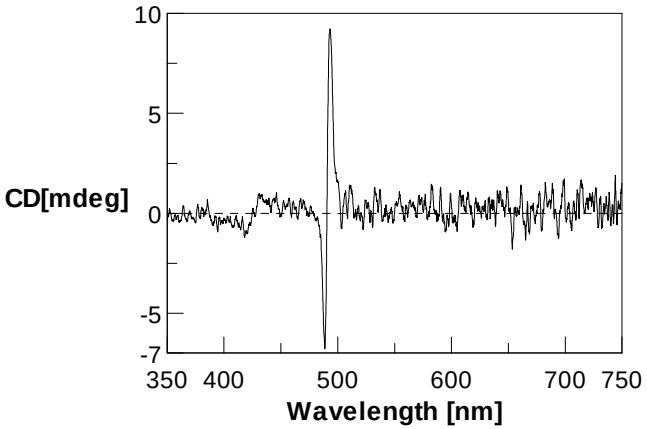
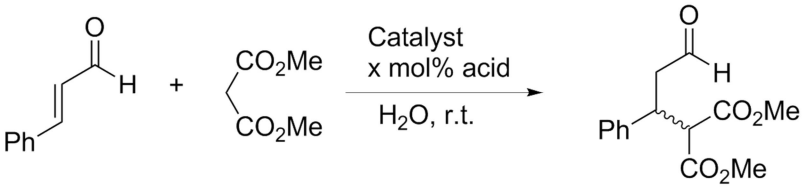


Figure 8**.** Circular Dichroism Spectrum of a zw-$TPPS_4$ solution ($4.07 \cdot 10^{-4}$ M) with an addition of 2 isoindoline equivalents, 66 µL from a 0,062M solution. Cell path 0.1cm.

5.4. CATALYSIS USING ZW-$TPPS_4$

To test the viability of using the prepared zw-$TPPS_4$ aggregate as a chiral anion for ACDC, two different organocatalytic reactions were carried out.

Michael reaction. A potentially suitable reaction that proceeds via an iminic intermediate that may be used to explore the viability of our approach is the well-known organocatalytic Michael reaction[9] (Scheme 9).



Scheme 9. Michael reaction schematic representation.

First of all, the possibility to use pyrrolidine as the organocatalyst was studied.

Table **6**. Set up of the Michael reaction with pyrrolidine as the organocatalyst.

Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[(a)]
1	pyrrolidine (10%)	pH 3.5[(b)]	24	3
2	pyrrolidine (10%)	pH 4.5[(b)]	24	6
3	pyrrolidine (10%)	TsOH (20%)	72	0
4	pyrrolidine (10%)	TsOH (10%)	72	0
5	pyrrolidine (10%)	TsOH (5%)	24	traces

[(a)] As inferred from the ^{1}H NMR of the reaction crude assuming a quantitative yield.
[(b)] Buffer AcOH/AcONa, 0.1M.

As so few or null product was obtained its isolation was not viable (Table 6), to check qualitatively the reaction yield the conversion was calculated using the crude reaction NMR (Figure 9).

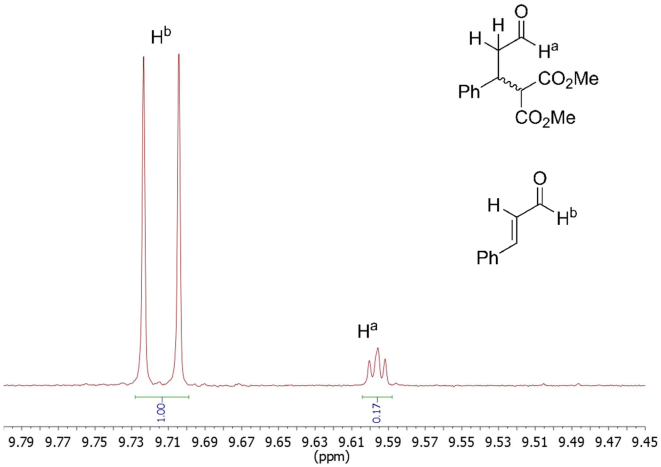


Figure 9. NMR example from a Michael reaction crude.

For the Michael reaction the conversion was calculated comparing the NMR signals of the doublet peak corresponding to the aldehyde proton from cinnamaldehyde, H^b, and the triplet peak corresponding to the aldehyde proton from the Michael product, H^a.

A very low conversion is observed in all cases. Only with the 0.1 M AcOH/AcONa buffer the reaction product can be significantly detected. As expected, a higher conversion is obtained at higher pH values. However, we need low pH values to mimic the acidic media in which the zw-$TPPS_4$ will be fully aggregated (compatible with the ACDC strategy). In order to mimic the effect of the sulfonatophenyl groups of $TPPS_4$, the experiments with TsOH were performed. The results are not promising because with the use of TsOH only at low concentrations of the acid the reaction product was detected. In any case, the reaction was tested under the ACDC conditions, comparing the effect of TsOH and zw-$TPPS_4$.

Table **7**. The effect of zw-$TPPS_4$ under ACDC conditions on the Michael reaction.

Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[(a)]
1	pyrrolidine (10%)	TsOH (10%)	72	0
2	pyrrolidine (10%)	zw-$TPPS_4$ (5%)	24	traces
3	pyrrolidine (10%)	Zw-$TPPS_4$ (5%)	120	traces

[(a)] As inferred from the ^{1}H NMR of the reaction crude assuming a quantitative yield.

Under ACDC conditions using the zw-$TPPS_4$ or TsOH (i.e. pyrrolidine/zwTPPS4 2:1 or pyrrolidine/TsOH 1:1) there was a very low or null conversion, and increasing the reaction time did not affect the result (Table 7).

Note that $TPPS_4$ has four 4-sulfonatophenyl acid groups, two of them contribute to the aggregate formation through Coulombic interactions to the centre pyrroleninic protonated nitrogen atoms of another porphyrin, so to correctly simulate the porphyrin effect two moles of TsOH are used for each $TPPS_4$ mol.

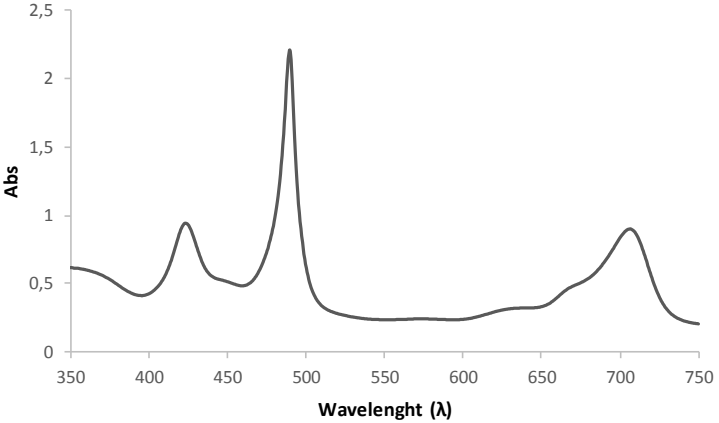


Figure 10. UV-visible spectra corresponding to the Michael reaction crude "entry 2" $TPPS_4$/pyrrolidine 2/1, under ACDC conditions.

Under the ACDC conditions the zw-TPPS4 in the reaction crude still strongly aggregates (Figure 10).

Table **8.** The effect of zw-$TPPS_4$ on the Michael reaction under different conditions.

Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[(a)]
1	pyrrolidine (10%)	TsOH (5%)	120	traces
2	pyrrolidine (10%)	zw-$TPPS_4$ (2.5%)	24	4

[(a)] As inferred from the ^1H NMR of the reaction crude assuming a quantitative yield.

Under these conditions an improvement on the conversion was observed when using zw-$TPPS_4$ (Table 8). This is probably due to the pH increase as checked before. Notice, however, that these are not ACDC compatible conditions as the 4:1 relation of base/porphyrin imply neutralization of the inner core of the porphyrin ring and, hence, the presence of important quantities of achiral monomeric species.

The previous experiments show that the pyrrolidine is not a good enough catalyst for the Michael reaction under the constraints imposed by our approach. Moreover, even if we move away from de ACDC conditions, the catalysis improves but is still very low.

After concluding that pyrrolidine was not a good enough catalyst, the next experiments were performed with isoindoline, also a secondary amine organocatalyst.

Table **9**. Set up of the Michael reaction with isoindoline as organocatalyst.

Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[a]
1	isoindoline (10%)	pH 3,5[b]	24	17
2	isoindoline (10%)	pH 4,5[b]	24	21
3	isoindoline (10%)	TsOH (10%)	24	8
4	isoindoline (10%)	TsOH (5%)	24	5
5	isoindoline (10%)	TsOH (2.5%)	24	17

[a] As inferred from the ^{1}H NMR of the reaction crude assuming a quantitative yield.
[b] Buffer AcOH/AcONa, 0.1M.

Better results are observed in the same conditions compared with the previous pyrrolidine experiments (Table 9), especially when using 0.1 M AcOH/AcONa buffer. Isoindoline presented a better conversion on media of higher pH values pointing to the fact that it is probably a better candidate to get good conversions in the acidic pH aqueous medium needed for the intended ACDC conditions.

However, when the corresponding experiments using the porphyrin (table 10) were performed a viscous precipitate was formed and the solution became transparent.

Table **10**. The effect of zw-TPPS$_4$ under ACDC conditions on the Michael reaction.

Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[a]
1	isoindoline (10%)	TsOH (10%)	24	8
2	isoindoline (10%)	zw-TPPS$_4$ (5%)	24	3
3	isoindoline (10%)	zw-TPPS$_4$ (5%)	96	6
4[b]	isoindoline (10%)	zw-TPPS$_4$ (5%)	72	8

[a] As inferred from the ^{1}H NMR of the reaction crude assuming a quantitative yield.
[b] The reaction was carried out on with a four-fold dilution.

In spite of adding the reagents when the aggregates were already formed, the formation of the precipitate evidenced some interference with the supramolecular chemistry (Table 10). Entry 4 was an attempt to minimize the problem. This approach worked, the solution did not flocculate, but conversion did not improve much.

Table **11**. The effect of zw-$TPPS_4$ on the Michael reaction without ACDC-compatible conditions.

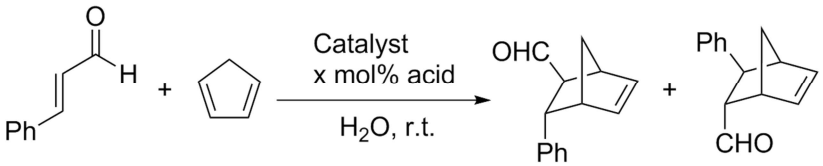
Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[(a)]
1	isoindoline (10%)	TsOH (5%)	24	5
2	isoindoline (10%)	TsOH (2.5%)	24	17
3	isoindoline (10%)	TsOH (2.5%)	96	23
4	isoindoline (10%)	zw-$TPPS_4$ (2.5%)	24	3
5	isoindoline (10%)	zw-$TPPS_4$ (1.25%)[(b)]	24	7

[(a)] As inferred from the ^1H NMR of the reaction crude assuming a quantitative yield.
[(b)] Neutralized $TPPS_4$

As seen before, if we move away from the ACDC conditions reducing the amount of TsOH, the conversion significantly rises. The conversion also improves with $TPPS_4$ but to a lesser extent, not so much the supramolecular problem still remains (Table 11).

In summary, it is not impossible for this Michael reaction to fit in the planned approach, but there is a very narrow window of suitable experimental conditions. The isoindoline gives, in general, a higher conversion but in $TPPS_4$ presence the mud-like phase formation is a big problem and for the TsOH experiments reveal that reducing its quantity, getting away from de ACDC conditions, the catalysis improves.

Diels-Alder reaction. Another potentially suitable reaction studied to explore the viability of our hypothesis is the Diels-Alder reaction. A well-known organocatalytic reaction amenable to the ACDC approach as it proceeds via iminic intermediate[10] (Scheme 10).



Scheme 10. Michael reaction schematic representation.

As seen on the experiments based on the Michael reaction, the pyrrolidine and isoindoline have different catalytic strengths, so the first experiments were aimed to choose which catalyst was better.

Table **12**. Influence of using pyrrolidine or isoindoline as organocatalysts on the Diels-Alder reaction.

Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[(a)]	Exo/Endo
1	pyrrolidine (10%)	-	48	2	42/58
2	isoindoline (10%)	-	48	12	32/68
3	pyrrolidine (30%)	pH 3.5[(b)]	120	15	45/55
4	isoindoline (30%)	pH 3.5[(b)]	96	10	42/58
5	pyrrolidine (30%)	TsOH (15%)	120	2	40/60
6	isoindoline (30%)	TsOH (15%)	96	24	57/43

[(a)] As inferred from the ^{1}H NMR of the reaction crude assuming a quantitative yield.
[(b)] Buffer AcOH/AcONa, 0.1M.

As so few or null product was obtained its isolation was not viable (Table 12), to check qualitatively the reaction yield the conversion was calculated using the crude reaction NMR (Figure 11).

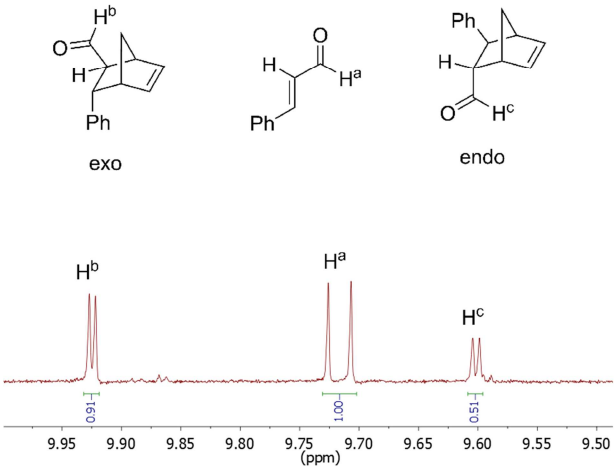


Fig. 11. RMN example from a Diels-Alder reaction crude.

For the Diels-Alder reaction the conversion was calculated comparing the NMR signals of the doublet peak corresponding to the aldehyde proton from cinnamaldehyde, H^a, and the doublet peaks corresponding to the aldehyde protons from both exo, H^b, and endo, H^c, product.

In the absence of acid, the reactions take place in both cases, though better with isoindoline. In 0.1 M AcOH/AcONa buffer the reaction takes place with similar results and with TsOH the isoindoline experiment had the largest conversion (Table 12). So the catalyst chosen to continue the experiments was isoindoline.

For the pyrrolidine experiments the endo form predominates, also for the isoindoline ones except in TsOH presence where there's a larger exo form ratio.

Next, the reaction was tested under the ACDC conditions, comparing TsOH and zw-$TPPS_4$.

Table **13**. The effect of zw-$TPPS_4$ under ACDC conditions on the Diels-Alder reaction.

Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[(a)]	Exo/Endo
1	isoindoline (30%)	TsOH (30%)	96	58	63/37
2	isoindoline (30%)	zw-$TPPS_4$ (15%)	72	18	59/41

[(a)] As inferred from the ^{1}H NMR of the reaction crude assuming a quantitative yield.

Under the ACDC conditions the Diels-Alder reaction shows very good results, but using $TPPS_4$ less conversion is obtained (Table 13), again the supramolecular chemistry is a problem as the reaction crude becomes a mud.

As seen in the previous TsOH experiment in this case also the exo form predominates, when porphyrin is the acid, this exo higher ratio remains but with a lower conversion, this fact suggest that the catalytic strength should come from the aggregate.

More friendly conditions for the supramolecular chemistry, with a lower concentration of all reagents, were tested in order to see whether or not the results above could be improved.

Table **14**. Optimization of the supramolecular chemistry.

Entry	Catalyst (mol %)	Acid (mol %)	Time (h)	Conversion (%)[(a)]	Exo/Endo
1[(b)]	Isoindoline (30%)	TsOH (30%)	96	3	29/71
2[(b)]	Isoindoline (30%)	zw-$TPPS_4$ (15%)	96	6	50/50
3[(b)]	Isoindoline (30%)	zw-$TPPS_4$ (30%)	96	2	57/43

[(a)] As inferred from the ^{1}H NMR of the reaction crude assuming a quantitative yield.
[(b)] The reaction was carried out on with a twelve-fold dilution.

The supramolecular chemistry problem was solved, but much of the catalysis strength was lost. So as the reaction conditions are so diluted on entry 3 was tested the possibility to work with an zw-$TPPS_4$ excess but it wasn't successfully, the medium is too acid (Table 14).

In summary, for the Diels Alder reaction there is a considerable window of experimental conditions under which the planned approach works. The experiments with isoindoline show that under ACDC conditions the zw-$TPPS_4$ catalysis works. As seen for the Michael reaction case, the supramolecular chemistry of the $TPPS_4$ becomes again a problem but not that bad, conversion ratios for the $TPPS_4$ experiments are higher, however diluting the crude reaction to improve the supramolecular chemistry also reduces the catalytic strength.

From the whole set of experiments, for the Michael and Diels-Alder reactions, it can be concluded that the ACDC approach is hard to make compatible with the required zw-$TPPS_4$ supramolecular chemistry conditions, yet not impossible, because there is a narrow window of experimental conditions in which it is worth to continue the exploration.

In summary. The results presented herein prove that the intended approach does indeed work under certain carefully controlled experimental conditions, which can still be further optimized, and that more work is needed to achieve larger conversions so that the reactions products can be effectively isolated and any possible enantiomeric excess evaluated.

6. EXPERIMENTAL SECTION

6.1. MATERIALS AND METHODS

All reactions and procedures were performed in solvents previously purified according to standard laboratory procedures.

6.1.1 Reagents used:

All reagents and starting materials were obtained from commercial suppliers and, unless specified otherwise, they were used without further purification.

Benzaldehyde (Acros, 98%), pyrrole (Aldrich, 98%, vacuum distilled immediately before use, 10 mbar, 35°C), propionic acid (Scharlau, 99%), sulfuric acid (Merck, 98%) hydrochloric acid (Sharlau, 37%), sodium bicarbonate (JEscuder), pyrrolidine (Aldrich, 99%), isoindoline (Acros Organics, 97%), cinnamaldehyde (Chemika Fluka, 98%, vacuum distilled immediately before use, 10mbar, 115°C), dimethyl malonate (Aldrich, 99%), toluenesulfonic acid (Merck, 98%), cyclopentadiene (Distilled from dicylcopentadiene (Acros, 95%), 42°C), sodium sulfate (Escuder), acetic acid (Scharlau, 99%), sodium acetate (Probus, 98%).

6.1.2. Solvents used:

Ethyl Acetate (Scharlau, extra pure), hexane (Scharlau), deuterated chloroform (Aldrich, 99.8%), methanol (Panreac, 99.9%, HPLC), dichloromethane (Lichorlsov, 99.9%, HPLC) and water of Milipore Q quality obtained with a Millipore Q-Gard was used throughout the purification procedures and for the preparation of all porphyrin solutions.

6.1.3. Equipment:

Balances

All the weights were measured with: Mettler Toledo PB 303-S Delta Range e=1mg, Mettler Toledo AB204-S e=1mg, Mettler Toledo AG245 e=0.01mg.

Rotary evaporators

To evaporate the solvent excess during the experiments, a Büchi Rotavapor R-200 was used, equipped with a rotational speed regulator and a thermostatized water bath to adequate the temperature on each case.

pH-Meter

pH measurements were performed on a CRISON Micro pH 2000 pH-meter (Crison 52-04 glass electrode) at room temperature. The pH-meter was calibrated prior to each measurement with standard buffer solutions at pH=7.00 and 4.00 (Metrohm).

Sonicator

The porphyrin aqueous solutions were sonicated, when necessary, with a Bransonic 321 sonicator.

Centrifugal device

Rotofix 32 A from Hettich was used to centrifuge the aggregate samples.

UV-Vis spectroscopy

UV-Vis spectra were recorded at room temperature on a double beam spectrophotometer: Cary-Varian 5E, which uses the software: Scan Varian. During the measurements, quartz Suprasil cells were used, with different optical paths: 10 mm x 10 mm, 10 mm x 1 mm, 10 mm x 0.1 mm and 10 mm x 0.01 mm Hellma.

Circular dichroism spectroscopy

Circular dichroism spectra were recorded at room temperature on a JASCO J-810 spectrometer, equipped with a 150 W Xe lamp (air cooled). During the measurements, quartz Suprasil cells were used with different optical paths.

Lyophilisation

The lyophilised samples were prepared at a vacuum pump cooled with an immersion cooler Crycool CC-100 II, filled with acetone at -80ºC.

Micropipettes

On the catalysis experiments, the reactants were added with micropipettes Brand and microsystems, with different possible volumes: 0.5-10 µL, 25-250 µL, 10-100 µL, 100-1000 µL.

Thin layer chromatography

Analytical thin-layer chromatography was performed on Merk silica gel or aluminum oxide plates (thickness of 0.2 mm) with fluorescence indicator (F254) and revealed at a UV lamp: Gomensoro S.A. λ=254.

^{1}H Nuclear Magnetic Resonance (^{1}H NMR)

The ^{1}H NMR spectra were recorded on a Varian Mercury 400MHz. Chemical shifts are referenced to the $CDCl_3$ signal (^{1}H 7.258 ppm downfield) relative to TMS at 0 ppm.

6.2. SYNTHESIS OF PORPHYRINS

6.2.1. Synthesis of 5,10,15,20-tetraphenylporpyrin (TPP)[7]

In a round bottom flask provided with a Dimroth condenser, 2.6 g of freshly distilled pyrrole (39 mmol), and 4.2 g of freshly distilled benzaldehyde (40 mmol) were dissolved under continuous magnetic stirring in 150 ml of propionic acid. After a while, the resulting mixture turned dark purple and was refluxed during 35 minutes. The reaction crude was filtered, the precipitate was washed with cold methanol. The dark purple crystals were recrystallized from dichloromethane/methanol to yield 20%, 1.215 g (1.94 mmols) of the title compound.

UV-Vis [(H_2O), λ(ε)]: 417(489100), 514(16700), 549(7850), 590(5700), 646(5100)

On the sample obtained there were some chlorin traces [7], see appendix 3, UV-visible figures.

6.2.2. Sulfonation procedure of 5,10,15,20-tetraphenylporpyrin[7]

An adapted procedure similar to that used to obtain the tetrasodium salt of the tetrasulfonated porphyrin was followed[7]. In a round bottom flask provided with a Dimroth condenser and a calcium chloride tube, 0.5g (0.8 mmols) of 5,10,15,20-tetraphenylporpyrin ($TPPS_4$) were slowly added to 7 mL of ice cooled concentrated sulfuric acid under vigorous magnetic stirring. The resulting green solution was heated to 100 °C for 6 h, cooled to room temperature and left under magnetic stirring for further 24 hours. From this point onwards, the

work-up and purification procedure was changed in relation to previously reported methods so as to obtain the zwitterionic form of the title compound.

6.2.3. Preparation of the zwitterionic form of 5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrin (zw-$TPPS_4$)

In order to obtain the zwitteronic form (zw-$TPPS_4$) of the title compound, the following optimized procedure was developed. The crude solution of 5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrin in sulfuric acid, obtained as described in the previous section, was poured onto 25 ml of water and a dark green precipitate was immediately formed. The precipitate was then transferred into a centrifuge tube and was centrifuged at 6000 rpm during 30 minutes. The supernatant solution was carefully removed and the precipitate was thoroughly washed (under stirring) with water and centrifuged again. The whole washing operation was repeated at least ten times until the pH of the supernatant solution was close to 1.5. At the end, the precipitate was additionally washed with 25 mL of an aqueous 0.1 M solution of HCl and then twice with water. The dark-green precipitate was lyophilized and 0.457 g (0.465 mmol), (yield 20%) of the title compound were obtained as a dark-green solid.

6.3. ORGANOCATALYTIC REACTIONS

All organocatalytic reactions were performed following a similar procedure to that described in the examples below. The small variations to explore the scope of suitable experimental conditions for the reactions can be inferred from the data presented in the tables of the Results and Discussion section.

6.3.1. Dimethyl 2-(3-oxo-1-phenylpropyl)malonate (1)[9]

On a 5ml round bottom flask, 24.6 mg (0.025 mmols) of the zwiterionic form of 5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrin ($TPPS_4$) and 1ml of miliQ water, 57 μL (0.5 mmols) of dimethyl malonate, 130 μL (1 mmols) of freshly distilled cinnamaldehyde, and 5.7 μL (0.05 mmols) of isoindoline were added in this order at room temperature under vigorous stirring. After 24 hours, the reaction crude is poured onto 7 ml of AcOEt, the organic layer is washed with a saturated solution of $NaHCO_3$ (2 x 10 mL). The combined aqueous phases are washed with 2 x 7 ml of AcOEt and finally the combined organic phases are washed with brine, dried

over Na_2SO_4 and the solvent is eliminated under reduced pressure to yield a dark-yellow oil. The crude mixture is analysed by ^{1}H-NMR as described in the *Results and Discussion* section.

6.3.2. *endo*-3-Phenylbicyclo(2,2,1)hept-5-ene-2-carboxaldehyde and *exo*-3-Phenylbicyclo(2,2,1)hept-5-ene-2-carboxaldehyde (2 and 3) [10]

On a 5ml round bottom flask, 73.8 mg (0.075 mmols) of the zwiterionic form of 5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrin, 1ml of miliQ water, 126 µL (1.5 mmols) of freshly distilled cyclopentadiene, 63 µL (0.5 mmols) of freshly distilled cinnamaldehyde and 17 µL (0.15 mmols) of Isoindoline were added under vigorous stirring. After 24 hours, the reaction crude is poured onto 7 ml of AcOEt, the organic layer is washed with a saturated solution of NaHCO3 (2 x 10 mL). The combined aqueous phases are washed with 2 x 7 ml of AcOEt and finally the combined organic phases are washed with brine, dried over Na_2SO_4 and the solvent is eliminated under reduced pressure to yield a dark-yellow oil. The crude mixture is analysed by ^{1}H-NMR as described in the *Results and Discussion* section.

7. CONCLUSIONS

With the results obtained in this project it has been shown that:

(1) zw-$TPPS_4$, free of any other anion, can be efficiently obtained in the gram-scale.

(2) zw-$TPPS_4$ does form chiral supramolecular aggregates which are stable when neutralized with two equivalents of an organic base (organocatalyst).

(3) thus, these acidic aggregates can be, in principle, used as catalysts in an asymmetric counter-anion directed approach in Michael and Diels-Alder reactions in water.

(4) it could be established that there exists a narrow window of experimental conditions in water in which the chiral supramolecular anionic aggregates are stable and some organocatalytic reactions via cationic intermediates can take place (i.e. Michael and Diels-Alder).

(5) however, for the Michael reaction only very low conversions were obtained.

(6) the Diels Alder-Reaction proved to be a more suitable reaction to further explore experimental conditions leading to higher conversions and product yields.

Overall, it has been proved that combining the research fields of self-assembling water soluble porphyrins (chiral sign selection by vortical stirring of supramolecular aggregates) and the asymmetric counter-anion directed strategy on organocatalysis can indeed be compatible under certain carefully controlled experimental conditions. With these results at hand, it is advisable to continue the exploration of this approach to see if it is eventually possible to transfer the macroscopic chirality of stirring into an enantiomeric excess of a chiral molecule.

8. REFERENCES AND NOTES

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9. ACRONYMS AND ABBREVIATIONS

UV-vis	Ultraviolet-visible
NMR	Nuclear Magnetic Resonance
TLC	Thin Layer Chromatography
HPLC	High Pressure Liquid Chromatography
Ppm	Parts per million
Rpm	Revolutions per minute
r.t.	Room temperature
CD	Circular dichroism
AFM	Atomic force microscopy
ACDC	Asymmetric Counteranion Directed Catalysis
3D	Three dimension
Equiv.	Equivalent
TMS	Tetramethylsilane
TRIP	3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate
AcOEt	Ethyl acetate
AcOH	Acetic acid
AcONa	Sodium acetate
TsOH	para-toluenesulfonic acid

APPENDICES

APPENDIX 1: CO_2 EFFECT

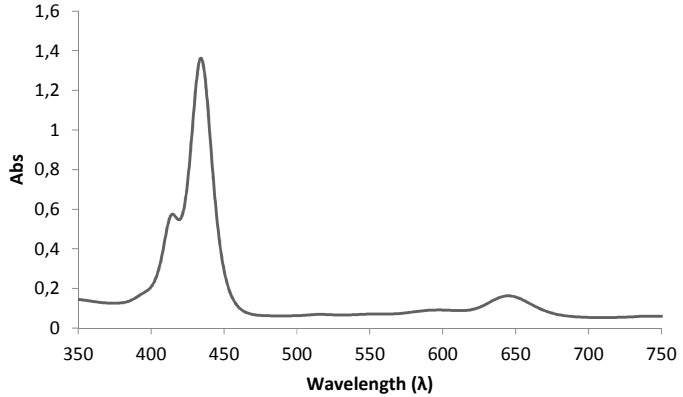


Figure 12. UV-visible spectrum of a zw-$TPPS_4$ $4.9 \cdot 10^{-6}$ M water solution.

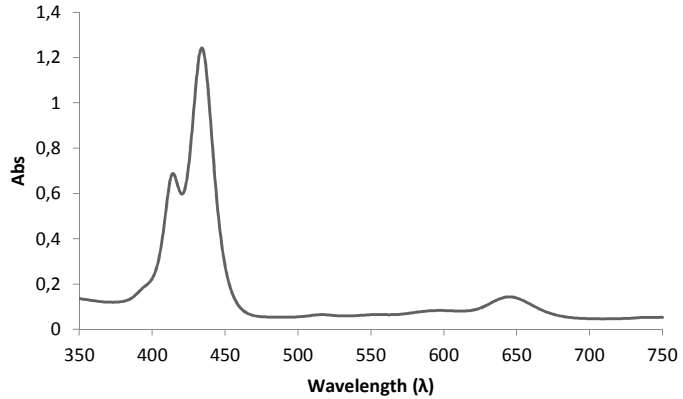


Figure 13. UV-visible spectrum of a zw-$TPPS_4$ $4.9 \cdot 10^{-6}$ M water solution after applying an N2 current during a few minutes.

APPENDIX 2: METHANOL EFFECT

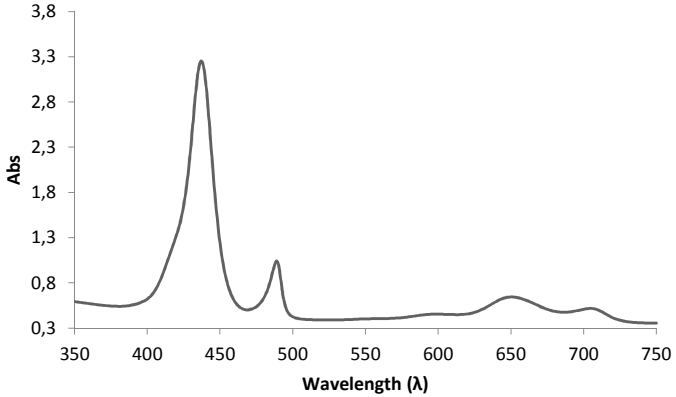


Figure 14. UV-visible spectrum of a zw-$TPPS_4$ ($5.2 \cdot 10^{-4}$ M) methanol solution. Cell path 1mm.

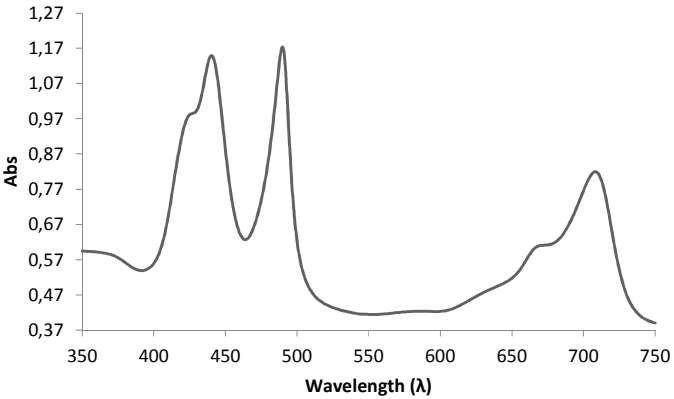


Figure 15. UV-visible spectrum of a zw-$TPPS_4$ ($5.2 \cdot 10^{-4}$ M) methanol solution, after a NaCl excess addition. Cell path 1mm.

APPENDIX 3: TPP UV-VISIBLE ANALYSIS

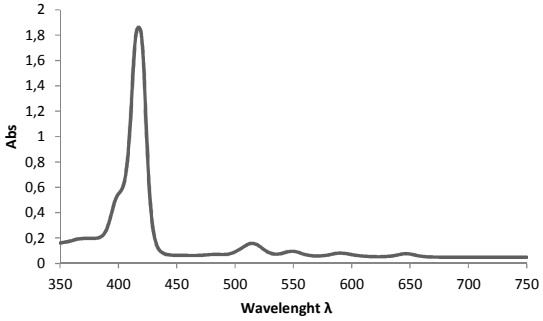
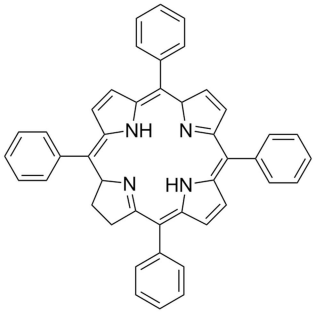


Figure 16. UV-visible spectrum of a TPP $7.6 \cdot 10^{-6}$ M water solution.



Scheme 11. Chlorin schematic representation.

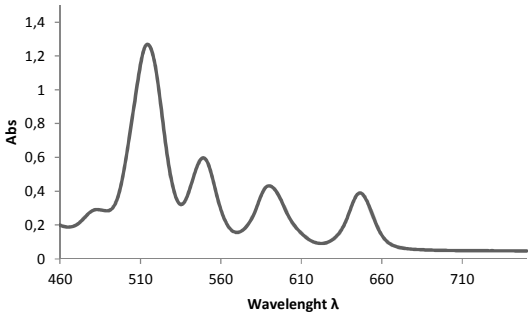


Figure 17. UV-visible partial spectrum of a TPP $7.6 \cdot 10^{-5}$ M water solution.

On the TPP synthesis some chlorin can be generated as a subproduct, its presence is detected by TLC and UV-vis. After the recrystallization process, the UV-vis. Spectrum evidences the presence of traces of chlorin as an increased absorption at 656 nm due to the superposition of the 645 nm band of TPP and the intense 651 nm band of chlorin[8].