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CICLO XXXI

Calixarene-based Viscosity Index Improvers and Detergents for Lubricants

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A Camerino,

«Nessuno può tornare indietro e ricominciare da capo, ma chiunque può andare avanti e decidere il finale».

Karl Barth

Contents

Abstract

Lubricants are made of two components: the base oils and the additives. Depending on the type of application, additives may be present from very small percentages up to the case of engine lubricants where the total additive content is usually somewhere between 5% and 30%. Additives, although present in lower percentages, can substantially improve the existing properties of the base oils and, moreover, can add new fundamental properties such as detergency, dispersancy and prevention from wear and corrosion. In order to try to answer to the growing requirements of the market both in terms of performances and environmental sustainability, the research in the field of additives is strongly pushing towards the discovery of novel molecules easy to be synthesised and possessing improved functions and properties. This study investigate the use of an innovative class of macrocycles, calixarenes, as starting point for the preparation of Viscosity Index Improvers and Detergents.

Calixarenes, the cyclic oligomers obtained by the condensation of *p*-substituted phenols and formaldehyde, were used for the synthesis of

Star Polymers (SP) to be applied as Viscosity Index Improvers, that are polymers able to modulate the viscosity of the base oils as a function of the temperature. SPs are structurally formed by two parts: a central core and a variable number of peripheral arms linked to the central structure. The approach used in this thesis for the preparation of SPs is the so-called "Arm-First approach" which consists to first prepare polymer arms via the Living Anionic Polymerisation and then to connect these preformed arms to a central core based on a *p-tert*-butylcalix[8]arene structure properly functionalised. After a purification step, the final product was tested and compared with other Star Polymers of well-known properties showing very good thickening power and good mechanical shear stability, a property very important for this kind of additives. Other calixarenes cores, able to react via a radical polymerisation with preformed arms were obtained and will be used in the preparation of Star Polymers with improved performances.

In the second part of this thesis, novel macrocycles derived from *para*-dodecylphenol and formaldehyde were synthesised, isolated and characterised by a combination of chromatographic separation and spectroscopy/spectrometry methods. The APPI-MS studies of the reaction products show the presence of calixarenes with different sizes and prevalence of calix[8]-, -[6]-, and -[5]arenes together with a smaller amount of linear oligomers. Also due to the long and inhomogeneous alkyl chains present at the upper rim of the macrocycle, the final products are liquid at room temperature. This prevents the easy separation of the macrocyclic components from the linear oligomers by simple precipitation. However, the yield of *p*-dodecylcalixarenes from the rather

cheap starting materials, is rather high (> 80%) and the mixture of macrocyclic (80%) and linear compounds (20%) was successfully used for the preparation, on a large scale, of overbased-detergents. This class of additives is used to neutralise the acid species and keep in suspension the polar compounds produced during the usage of the lubricants in the engine. Thanks to these new macrocycles it is possible to obtain detergents having very high values of TBN (Total Base Number) and very good detergency properties, indicating a rather high quality of these calixarene-based additives.

Abbreviations

ACN = Acetonitrile

API = American Petroleum Institute

APPI-MS = Atmospheric Pressure Photoionization Mass Spectrometry

ASTM = American Society for Testing and Materials

BrAcOEt = Ethyl Bromoacetate

BuLi = Butyl Lithium

CCS = Cold-Crancking Simulator

COF = Coefficient Of Friction

COSY = Correlation Spectroscopy

CuAAC = Copper(I)-Catalyzed Alkyne-Azide Cycloaddition

DBN = Direct Base Number

DCM = Dichloromethane

DMF = N,N-Dimethylformamide

DMSO = Dimethylsulfoxide

ESI-MS = Electrospray Ionization - Mass Spectrometry

Et_2O = Diethyl Ether

EtOAc = Ethyl Acetate

EtOH = Ethanol

FM = Friction Modifier

FR = Friction Reducer

GC-MS = Gas Chromatography - Mass Spectromerty

GMS = Glycerol Monostearate

GPC = Gel Permeation Chromatogrphy

HPLC = High Performance Liquid Chromatography

HSQC = Heteronuclear Single Quantum Coherence Spectroscopy

IPC-AES = Inductively Coupled Plasma - Atomic Emission Spectrometry

MALDI-TOF = Matrix Assisted Laser Desorption Ionization - Time-of-Flight

MALLS = Multi Angle Light Scattering

m-CPBA = 3-Chloroperbenzoic Acid

MeoH = Methanol

MW = Microwave

NMR = Nuclear Magnetic Resonance

NTU = Nephelometric Turbidity Unit

PAOs = Poly-Alpha-Olefins

PDP = p-Dodecylphenol

PM = Particulate Matter

PPD = Pour Point Depressant

R_F = Retention Factor

SAE = Society of Automotive Engineers

SSI = Shear Stability Index

TBN = Total Base Number

tBuOK = Potassium tert-Butoxide

TEOST = Thermo-oxidation Engine Oil Simulation Test

THF = Tetrahydrofuran

TLC = Thin Layer Chromatography

UTF = Ultra-Thin Film Measurement System

VHVI = Very High Viscosity Index base oil

VII = Viscosity index Improver

VM = Viscosity Modifier

Chapter 1

Lubrication and Lubricants

1.1 Introduction

Lubrication is the operation that allows friction and wear, arising from two surfaces moving in extensive contact, to be reduced. The first one, friction, is the force opposing to the motion of the two bodies in contact. The main drawbacks of friction to be reduced are the formation of heat and the consumption of energy. On the other hand, wear, is a process that leads to a continuous loss of material. It depends from corrosion, abrasion and other events that cause modifications of the morphology of the surfaces of the two bodies in contact.

There are examples where it may be desired to reduce mainly one of these events, but in many applications it is necessary to reduce both and this could be obtained by lubrication.

Lubrication is very important; it has a considerable impact in the correct behavior of machines and mechanical systems. If carried out correctly it helps their proper functioning, improving the general performance of the

machine, reducing waste of energy and deterioration of the components. Instead an unsuitable lubrication can lead to malfunctions, loss of energy and damages. So it is clear that lubrication is linked to economic benefits in the form of energy-savings, conservation of materials, reduction of costs in maintenance operations. Especially in the latest years, lubrication is especially studied and encouraged because of its positive effects on environment both in terms of saving of fuel/energy and reduced pollution. It is therefore playing an important role for environmental sustainability.

The main principles of lubrication have been known since ancient times, but modern lubrication bore in the second half of the nineteenth century during the second industrial revolution. Since then, lubrication was developed and a great amount of innovations were introduced. The most recent studies revealed that there are new areas to be investigated, with promising potential applications, and showed that research in the area of lubrication is still alive and challenging.

1.1.1 Methods of Lubrication

The simplest way to reduce friction and wear is to place between the two surfaces in contact a substance that allows their relative motion more easily. This purpose can be achieved by placing a fluid film having high resistance on the two surfaces in order to keep them apart and to reduce friction and wear.

There are three main methods of lubrication: fluid film lubrication, boundary lubrication and mixed lubrication. They are characterised by different friction and wear situations and are generally discriminated by a

parameter λ, that is defined as the ratio between the thickness of the film and the average roughness of the surfaces.

- *Fluid-film lubrication (hydrodynamic lubrication)*: this is the simplest situation which originates when the lubricating film is thick enough to effectively separate the two surfaces, preventing a direct contact between the two bodies. This situation is typical of contacts with low loads or with highly viscous liquids, and the lubricating peculiarities depend on the properties of the lubricant. The viscosity of the lubricant determines the friction coefficient. The thickness of the fluid film is higher with respect to the asperities of the surfaces, so the parameter λ has a value from 5 to 100.
- *Boundary lubrication*: in this regime the lubricating film is thinner and eventually reaches a condition where the thickness is similar to the height of the asperities on the metal surfaces. The roughness and the composition of the surfaces influence mostly the resulting friction, while the viscosity plays a little part in the frictional behavior. It is a method of lubrication that can be found in various types of contacts characterised by very high load in relation to the speed of the surfaces. The thickness of the layer is very small compared to the roughness of the surface so the parameter λ is less than 1.
- *Mixed lubrication*: it includes both of the methods already illustrated. It arises when in the contact there are areas in which the surfaces are very close to each other where boundary lubrication is required, together with areas in which fluid-film lubrication

prevails. This is a very widespread method of lubrication, used in many machines elements such as gears, roller and ball bearings. Parameter λ has a value between 2 and 5.

1.1.2 Action of the Lubricant

Different operation modalities require different methods of lubrication also for the same mechanical connection. It is possible to understand this consideration observing the Stribeck Curve in *Figure 1* in which friction (μ) is a non-linear function related to a dimensionless parameter given by the product of the oil viscosity (η) for the relative speed (v) between surfaces divided by the load (*p:* force per unit of length).[1]

The Stribeck curve exemplifies one basic effect that lubricant viscosity has on friction: reducing oil viscosity lowers viscous drag in hydrodynamic lubrication, but will eventually increase friction when the

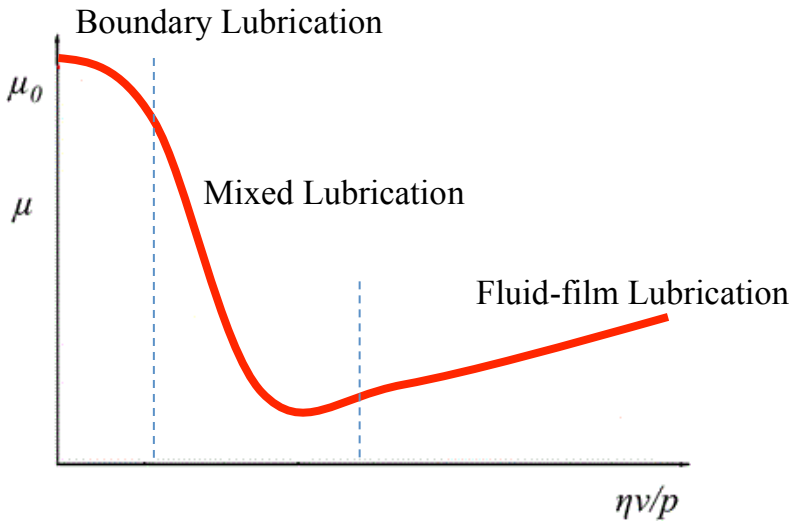


Figure 1 – Friction coefficient as a function of the relevant operational variables (Stribeck Curve).

film thickness becomes so thin that solid-to-solid contacts begin to occur in the mixed lubrication regime and reaches a maximum in the boundary lubrication regime.[2] Thanks to its physical-chemical properties, lubricants can affect the coefficient of friction through formation of the surface films thus creating the best conditions of operation for the engines.

When there are two surfaces very close in which there is also contact between the asperities of the surfaces, the lubricant performs its function by forming a little thin film on the two layers. The formation of the film is due to the van der Waals forces among the polar molecules of the lubricant and the solid surfaces. In this way the layer is formed by molecules linked at one extremity to the surfaces, which can easily slide over each other. All liquid lubricants have pretty much this ability, however it can be improved by using specific additives. These are made up of long chain molecules, provided with a polar head (for example fatty acids, esters and amides) through which they are anchored by chemical adsorption to the metal oxides of the surfaces, keeping the remaining part of the molecule unchanged. This gives rise to layers with a high sliding power which produces little friction, creating resistance to crushing. The resistance of this layers is moderate, it can be used with only low loads and in a little range of temperatures.

More resisting films can be obtained mixing some commonly-used additives into anti-wear lubricating oils. These compounds contain sulfur, phosphorus and metals with a very limited thermal stability, so for the effect of the temperature they decompose and form a protective layer on the surfaces. This layer is composed by amorphous material and it guarantees a lubrication to medium temperatures and load.

It is possible to create even more resisting layers using a kind of additives called Extreme Pressure additives. These additives contain compounds with sulfur and phosphorus, and their great ability derives from their tendency to react with the metal surface to form inorganic salts with high melting points (600-700°C). These additives are able to perform lubrication also under very extreme conditions.

1.1.3 Lubricants with a different state of aggregation

The most widespread lubricants are liquid, however there are situations in which a different state of aggregation of the lubricant is needed, in order to achieve particular properties.

Gaseous Lubricants: they are formed by gas such us air, nitrogen and helium. They are very stable and are able to maintain their state of aggregation in a large range of temperatures and for these reasons they have advantages in respect to the liquid lubricants. They can be used at very low temperatures or very high ones.

Another important feature is their low viscosity that determines extremely limited friction values. Not only, as opposed to liquids, their viscosity increases with increased temperatures so they do not lose their capacity to support the load due to overheating.

Solid Lubricants: the surface layers of these lubricants is composed by laminated aggregates able to slide over each other or by smooth molecular conformations. Graphite and molybdenum disulfide (MoS_2) are the prevalent materials used as solid lubricants. They are applied in situations in which it is not possible to use liquid lubricants, like in vacuum or

in high-temperature lubrication conditions where oxidation and decomposition of the liquid lubricant will occur. However they present some disadvantages, firstly their efficiency is influenced by the difficulty of maintaining a sufficient layer of lubricant, secondly their protection against wear is sometimes limited. In fact if the solid layers breaks it is not self-regenerating like in the case of liquid lubricant films.

Semisolid Lubricants (lubricating greases): these are solid or semisolid products formed by two part, the first one is a lubricating oil while the second one is a dispersed solid phase that gives the thickening power to the lubricant. Lithium, sodium, calcium and aluminum soaps are generally used as thickening agents. Their applications are limited by the phase changes (fusions) that take place at various temperatures. For applications at very high temperatures thickeners with high melting points are used, such as polyurea.

The thickening agents give firmness to the grease. With this ability the lubricant remains by itself on the mechanical connection to be lubricated without requiring auxiliary devices. Furthermore it prevents the access of dangerous substances like dust and humidity. The main use of greases is for lubricating machine elements such as gears and bearings.

Liquid Lubricants: these lubricants are the most used ones because they can satisfy many needs in a great amount of applications. This is possible because they possess both lubricating function and also a series of secondary desirable functions. Considering the various number of classes of liquid lubricants, they can cover a temperature range of work from about -60°C to 250°C. They are also able to work with all the methods of lubrication: fluid-film, boundary and mixed. In boundary

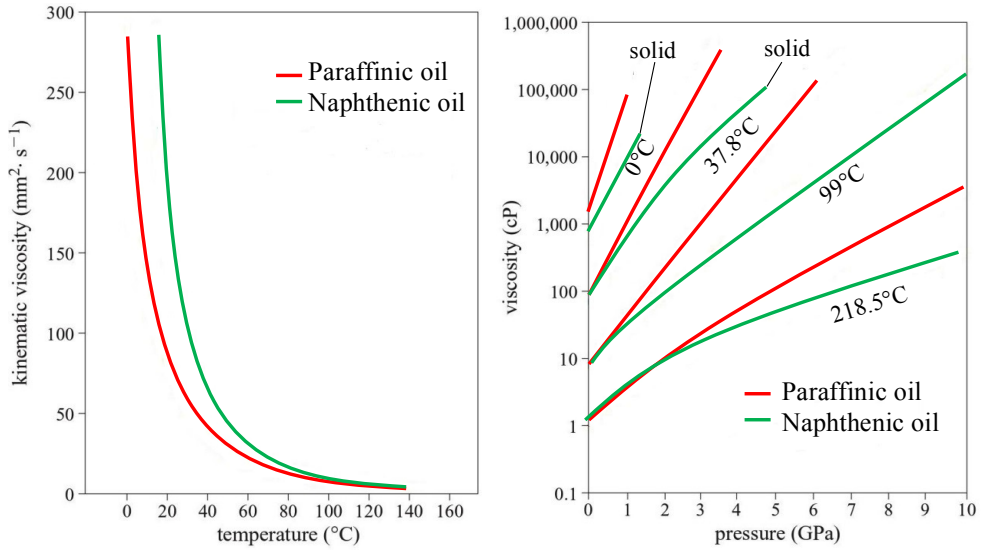


Figure 2 – On the left: Viscosity-temperature diagram of liquid lubricants. On the right: Viscosity-pressure diagram of liquid lubricants.

lubrication, performance is basically determined by the chemical and chemical-physical properties of the base liquids, sometimes increased with the addition of specific additives. Under such conditions these lubricants form a film on the surfaces, which creates the last barrier preventing contact between the solids. On the other hand, in the fluid-film lubrication, the performance of lubrication of the liquid is related to its rheological properties; among them the most important is viscosity because determines the friction coefficient. Viscosity is influenced by three physical parameters present in mechanical connection: temperature, pressure and shear stress. *Figure 2* shows the dependence of viscosity from temperature and from pressure; for the first one when temperature increases viscosity drops sharply with loss of the capacity to sustain the load, thereby increasing the risk of seizure. Pressure, on the other hand, exercises a positive effect on viscosity, with favourable consequences for

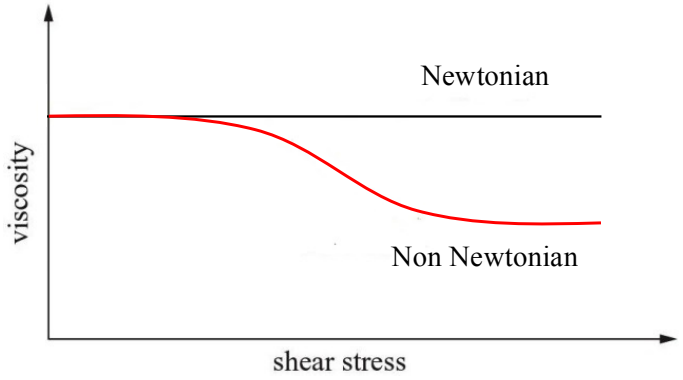


Figure 3 – Liquid lubricant viscosity as a function of shear stress.

lubrication. Instead the relationship between viscosity and shear stress is illustrated in *Figure 3*. When the shear stress increases, lubricants can follow two different behaviors depending on the interactions among the molecules. The first case is called "Newtonian fluid" and it arises with little combined liquids, such as base oils also containing simple additives: in this situation viscosity is not affected by shear stress. In the second case, instead viscosity decreases when the shear stress increases, this is called "Non Newtonian fluid" or "Pseudoplastic". This effect determines a reduction in the capacity to support the load and it is reversible within certain stress limits only, beyond which it becomes permanent.

An essential feature of liquid lubricants is its ability to maintain the performance for the required time. This is due to both the chemical and physical stability of the lubricant. Other important functions of the liquid lubricants are: heat removal, the capacity to remove and to transport fragments of worn material or solid contaminants and protection against corrosion.

The last aspect of liquid lubricants is the possibility to treat them with chemical additives in order to improve their properties. With the use of additives it is possible to create lubricants able to satisfy all the requirements of the different applications.

1.2 Main components of Lubricants for vehicles

Lubricants perform a large number of functions. The most important are lubrication, cooling, cleaning and protection of metal surfaces against corrosion.[2–5]

Lubricants comprise a base oil and additives. The base oil can have different origins; it can be mineral, biological or synthetic. Its main function is lubrication but it also works as carrier for additives. Additives increase the already-existing properties of the oil such as viscosity and oxidation stability, or add new properties like detergency, dispersancy, wear and corrosion control. Some classes of additives are premixed and added to the lubricating oil in the form of an “additive package”.

The enhanced properties in a lubricant are chosen in respect to the application, for example automotive use requires lubricants with good oxidation stability and high viscosity index; conversely metalworking lubricants need good cooling ability and corrosion control.

1.2.1 Base oils

The term base oil is used to describe base fluids originating from crude oil. The properties of the various base oils are influenced by their hydrocarbon chemistry.[6] The hydrocarbon structures present in base oils are paraffins, naphthenes, olefines and aromatics (*Figure 4*). Paraffins are straight and linear hydrocarbons; if there are side chains to the linear hydrocarbon they are called iso-paraffins. Instead naphthenes contain ring structures and olefins (unsatured hydrocarbons) are characterised by the presence of at least one double bond. The distribution between the chemical structures changes among different base oils, giving them particular properties.

The qualities of base fluids is influenced not only by their chemical structure but also by their molecular weight distribution. In general, a narrow molecular distribution means more predictable properties. Volatility, solvency, polarity, oxidation stability and viscosity of the final

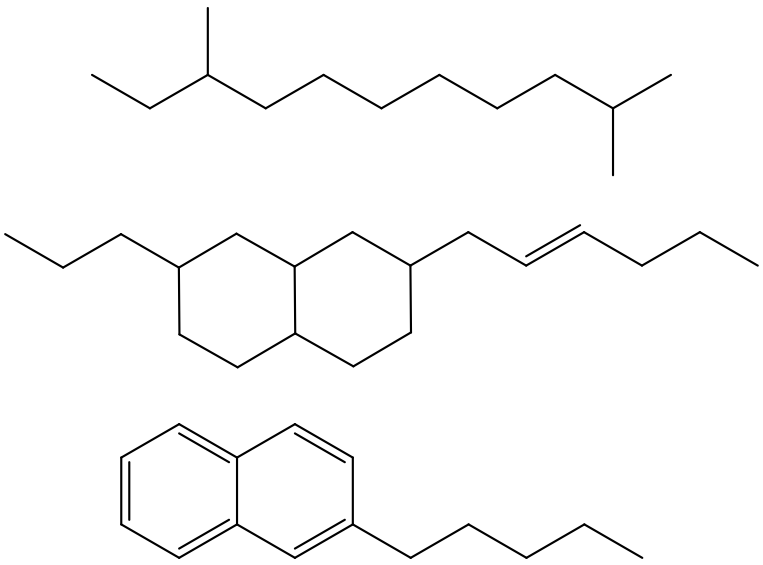


Figure 4 – Iso-paraffins (top), naphthenes (middle) and aromatics (bottom).

lubricant are influenced by the type of base oil. There are three main classes of base oils: mineral bases, non-conventional mineral bases and synthetic bases.

Mineral bases: they are hydrocarbons that are originated from the crude oils and contain mixtures of n-paraffins along with isoparaffins, cycloparaffins and aromatics having about 15 or more carbon atoms. The presence of the aromatic compounds determines its good solvent capacity (solvency). They also present a good oxidation stability thanks to the sulfur compounds which act as natural antioxidants. They have inferior properties if compared to the synthetic bases, because of the higher content of n-paraffin which determines very high viscosity index. In addition, they possess great volatility that contributes towards rapid deterioration of the lubricant.

Non-conventional mineral bases or Very High Viscosity Index Base Oils (VHVI): the process used to produce this kind of base oil gives better characteristics compared to the mineral bases. They are treated with hydrogen to remove double bonds and to break up cyclic structures in the hydrocarbons. VHVI base oils consist of mainly paraffinic structures, even though naphthenic structures also occur. Compared to the mineral base, they present some advantages: lower volatility, higher viscosity index, better stability to temperature and low or negligible sulfur content.

Synthetic bases: polyalphaolefins (PAOs) are the main class of synthetic bases. They are synthesised from linear paraffins and they are a mixture of saturated hydrocarbons with a high degree of branching. The synthesis produces a base fluid of well-defined molecular structure with a very narrow molecular weight distribution. This structure donates good

Group	Saturation (% wt)	Sulfur (% wt)	Viscosity Index
I	<90	and/or >0.03	80-120
II	≥90	≤0.03	80-120
III	≥90	≤0.03	≥120
IV	PAOs		
V	All other bases		

Table 1 – API classification of base oils.

properties both at high and at low temperatures. Furthermore PAOs have high viscosity index, low volatility and good oxidation stability. However they are not very polar and so they are not able to solubilise the most polar additives. To avoid this problem, PAOs are generally mixed with esters, another class of synthetic bases, that confer the necessary polarity.

Base fluids are categorised into Groups I, II, III, IV and V according to API classification. They are classified in relation to the content of sulfur and saturated compounds and to the viscosity index (*Table 1*). Mineral bases are distributed among the Groups I, II and III. VHVI bases are of the Group III and PAOs of the Group IV. Esters are the most important base oils that belong to Group V.

1.2.2 Additives

Nowadays additives are essential for the proper performance of mechanical engines and to extend the lifetime of the lubricant. Without additives, lubricant would degenerate rapidly due to the corrosion and to the wear.

The additive content in lubricating oils ranges from just a few parts per million to several percentage points (maximum 30%). There are different classes of additives, the most important are: viscosity index improvers, detergents and dispersants, friction modifiers, pour point depressants and oxidation inhibitors.

Viscosity Index Improvers

Viscosity Index Improvers (VIIs) are a class of molecules, generally polymers, with very high molecular weights and able to influence viscosity of the oil at all temperatures.[7] As explained in section *1.1.3*, the viscosity of the base oil drops when temperature increases, however VIIs influence this trend. They slow down the decrease of viscosity thanks to the changes of conformation of their structure.

The structure of VIIs is similar to a "coil". When temperature starts to increase (*Figure 5*), the coil size expands and occupies a bigger volume, this process contrast the loss of viscosity of the base oil. Instead at low temperatures the coil is present in a "contracted" structure so that, in consequence, their influence on viscosity is low and the viscosity of the base oil prevails.

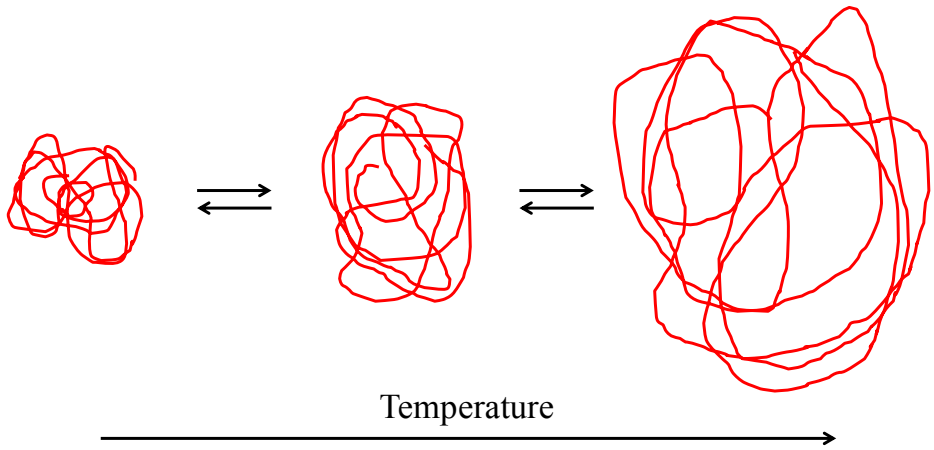


Figure 5 – Expansion of the VII with the increasing of the temperature.

In the production of the VIIs, control of the molecular weight and its distribution are the two most important parameters because they influence two basic properties of the additive, its thickening power and its mechanical shear stability.

The mechanical stability is an essential feature for a VII. In fact high molecular weight molecules are the most efficient thickeners but they are very susceptible to the shearing effects. A lubricant during its operation under mechanical stress is subject to great shear effects, so the mechanical shear breaks the polymer chains of the VII causing a permanent loss of viscosity. Polymer chain rupture occurs through homolytic cleavage of a carbon-carbon bond, being statistically favored in the central positions of the polymer chain. The cleavage produces two molecules with roughly an half of the initial molecular weight. The contribution to viscosity of the two smaller molecules is therefore less than that of the original one. *Star Polymers* are a class of Viscosity Index Improvers that are less influenced by shearing effects and their properties and characteristics will be discussed in *Chapter 3*.

The main polymers constituting VIIs are: hydrogenated ethylene-propylene copolymers,[8] polymetacrylates,[9] hydrogenated styrene-diene copolymers and hydrogenated polyisobutenes.

Detergents and Dispersants

Detergents and Dispersants belong to the class of the deposit control agents. They are very important additives for the lubricant and they have two functions, keep clean the engine (detergents) and keep in solution the insoluble contaminants avoiding deposits (dispersants).

In engine oils, one of the first causes of degradation comes from the combustion of the fuel which gives rise to hydroperoxides and free radicals.[10] The fuel combustion products pass through the piston rings into the lubricant as blowby and starts to attack the lubricant hydrocarbons causing their oxidation and degradation. This reactions of decomposition generates many species such as aldehydes, ketones and carboxylic acids.[11–13] These substances undergo different reactions in the lubricant and create different kind of deposits. Common types of deposits are varnish, lacquer, soot and sludge.[14,15] These insoluble materials could lead to malfunctions and could clog small openings in the engine. Furthermore acids have the tendency to attack metal surfaces causing corrosive wear. Detergents and dispersants are added to the lubricant to limit this kind of phenomena.

Detergents are used to neutralise the acid species. They are metal salts of organic acids that frequently contain associated base in excess. The acids normally used to synthesise these compounds include arylsulfonic acids, alkylphenols and carboxylic acids such as fatty carboxylic acid.[16]

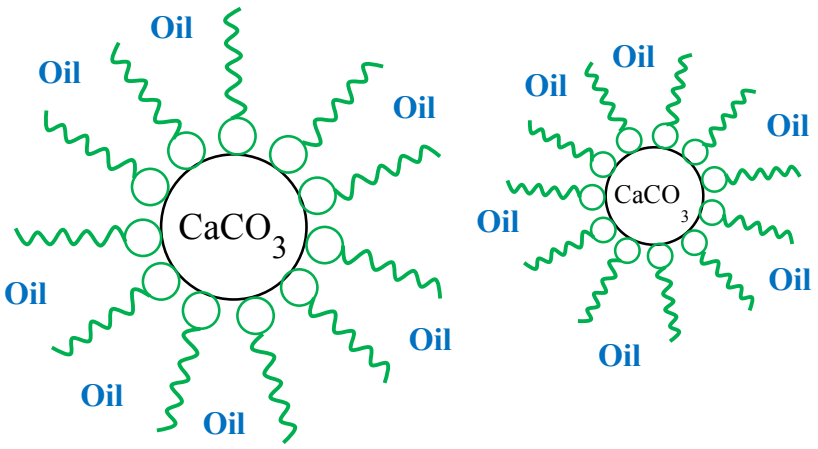


Figure 6 – Example of detergent structure.

The reaction of these acids with inorganic bases result in the formation of the salts. The most used metals in the formation of the detergents are calcium and magnesium. If the metal is present in stoichiometric amount gives rise to neutral salt also called "soap". If the metal is present in excess the detergents are called basic, overbasic or superbasic. The final structure of the detergent is a reverse micelle (*Figure 6*) in which the core is the base, generally in the form of carbonate, while outside there are the organic salts that thanks to their amphiphilic nature are able to suspend in the oil the excess of base.

Dispersants avoid the precipitation of the polar compounds generated by the combustion of the fuel in the engine. They are amphiphilic molecules composed of a polar group, usually nitrogen or oxygen, and by a lipophilic portion consisting of polyolefinic chains (generally polyisobutene).[3] Dispersants interact through the polar moieties with the insoluble particles and thanks to the lipophilic chains keep them in solution including the undesirable polar species into micelles (*Figure 7*),

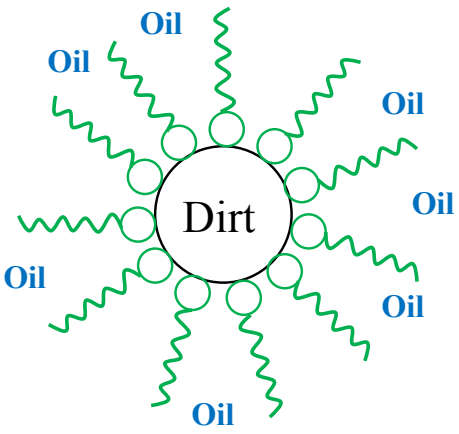


Figure 7 – The contaminants are caught by the dispersants in a micelle structure.

they prevent agglomeration between these particles that lead to the formation of deposits.

Friction Modifiers

About 25% of the energy supplied by the fuel is absorbed by the processes of mechanical friction that take place in the engine contacts. The lubricant can exercise a significant role in limiting this phenomenon and thus significantly contributing to the "Fuel Economy", that is the reference parameter for assessing energy saving. One of the options for reducing friction is the use of chemical additives called Friction Modifiers (FM) or Friction Reducers (FR). These additives are chemical species able to influence friction coefficient. They may consist of very long amphiphilic organic molecules with a polar head[17,18] or of metal-organic compounds (generally with molybdenum).[18–21] The reduction of the friction coefficient of the surfaces takes place by means of the formation of an extremely smooth film of molecules over them, through a mechanism similar to that illustrated in section *1.1.2*.

Antioxidants

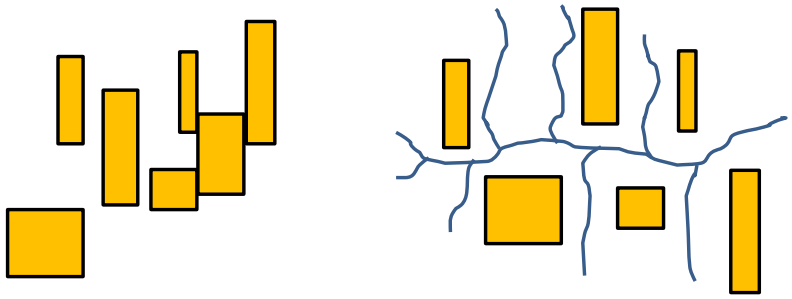
Oxidation is the result of the interaction of oxygen with the components of the lubricant at the temperature of operation of the engine. Oxidation produces harmful species that can impair the functionalities of the lubricant and damage the mechanical parts of the engine. The oxidative degradation of the lubricant occurs due to a complex series of radical chain reactions, which can be stopped by the use of antioxidant additives or oxidation inhibitors. These additives explicate their function thanks to two different mechanisms. In the first one they interrupt the chemical reaction responsible of the formation of the radicals, in the second one they decompose the primary products of degradation preventing any further evolution towards more dangerous species.

The main types of this class of substances are sulfur compounds,[22] alkylated aromatic amines[23,24] and sterically hindered phenols.[25]

Pour Point Depressants

These additives improve the pour point characteristics of the lubricant at low temperatures.

Lubricant viscosity increases when cooling the lubricant. At a certain temperature the lubricant becomes before cloudy and then solid and loses its flow characteristics. This happens because the lubricant starts to crystallise (forming waxes) resulting in a rapid increase of the viscosity. Pour Point Depressants (PPDs) avoid this rapid increase in viscosity. They have a polymeric comb structure, that is characterised by long chains grafted in the polymer backbone and interspaced by shorter chains. The long aliphatic chains interact with the waxes in the oil while the shorter



Oil without PPD Oil with PPD

Figure 8 – Effect of the Pour Point Depressant on the base oil.

chains act as inert diluents and help to control the extent of wax interaction. In this way, PPDs can prevent the wax aggregation, maintaining the system fluid at low temperatures.[26] The main types of PPDs are: polymethacrylates,[27] ethylene-vinyl acetate copolymers[28] and polyfumarates.[29]

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Chapter 2
Calixarenes

2.1 Introduction

Calixarenes[1–3] are macrocycles which derive from the condensation of phenols and formaldehyde in different conditions. They are composed by a number of aryl units that is generally comprised from 4 to 8. The name "Calixarene" was coined by C.D. Gutsche[4] in 1978 and is composed by the prefix "Calix", meaning vase in Greek, and by "arene" as a suffix, denoting the presence of aryl residues in the cyclic array.

They became popular during the growing phase of the supramolecular chemistry because there was a demand of accessible and synthetically versatile units for the construction of receptor molecules of increasing complexity, able to execute special supramolecular functions. Calixarenes have both these qualities, in fact they can be acquired by one-pot syntheses in good yields and can be simply functionalised both on the phenolic OH groups and on the aromatic nuclei. Moreover the

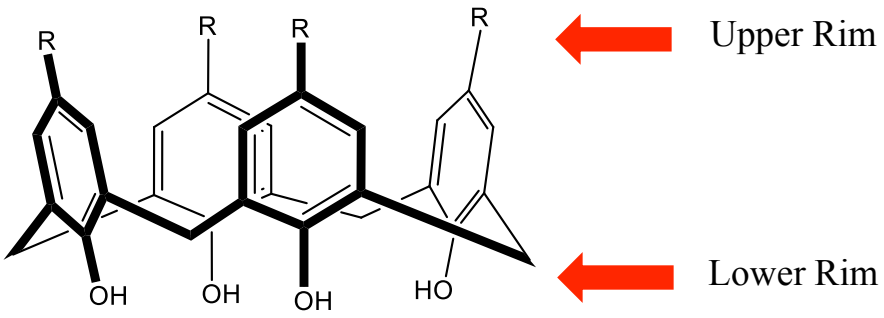


Figure 9 – Calix[4]arene in cone conformation.

conformational properties of these macrocycles can be used to create new shapes and architectures for molecular receptors.

The chemistry of the calixarenes was investigated mostly with the cyclic tetramer. This compound assumes, in the native form (all the phenolic OH unfuctionalised), a conformation in which all the aryl units are oriented in the same direction. This conformation is called "cone" and is the one usually observed in the solid state and in solution when free phenolic OH groups are present, because of strong H-bonding among them.

Referring to the cone structure of the calix[4]arene (*Figure 9*), two domains can be identified, the para position of the aromatic rings and the phenolic OH groups area, which are called respectively the "upper rim" and the "lower rim" of the calix.

At low temperatures, the ^{1}H NMR spectrum of the calix[4]arene shows a doublet for the hydrogens of the methylene bridge, but at high temperatures the signal becomes a singlet. This behavior is due to the interconversion between two mirror images in cone conformation of the calix[4]arene. At low temperatures this equilibrium is slow, respect to the NMR time scale, while at high temperatures it is faster.[5] Tetramethoxy and tetraethoxy calix[4]arenes are also conformationally mobile but with

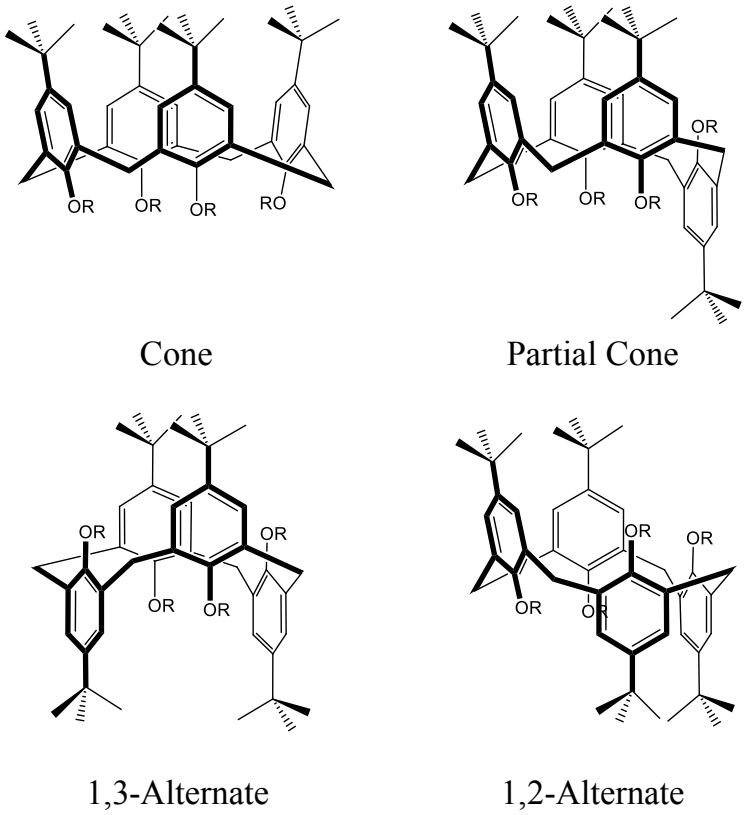


Figure 10 – Different conformations of calix[4]arene derivatives (R > Et).

the introduction at the lower rim of alkyl groups bulkier than ethyl, the ring inversion process is blocked and this lead to the formation of compounds with different stereochemistry. The different orientation of the aryl groups generate four limiting structures that were named by Gutsche: *cone*, *partial cone*, *1,3-alternate* and *1,2-alternate* (*Figure 10*).[6]

When the number of phenolic units grows ($n \geq 5$), the conformational mobility of the macrocycle in solution increases. In these situations the macrocycle is often present as a mixture of conformers with similar energies that rapidly interconvert each into the other. Calix[5]arenes can be conformationally arrested by functionalisation at the lower rim,[7–9]

but this becomes more difficult for calix[6]- and calix[8]arenes, although few examples have been reported in literature.[10–12]

2.2 Synthesis of Calixarenes

For many years the preparation of *p-tert*-butylcalix[4]arene remained a capricious event. In some instances were obtained good yields of the desired product, while other times poor yields or no yields were obtained under, apparently, similar conditions.

Nowadays the most used approach for calixarene synthesis is the "base-promoted one-step-synthesis". *p-tert*-Butylcalix[4]arene can be synthesised in bulk quantities following the procedure originally formulated by Zinke[13] and then modified by Conforth[14,15] and later by

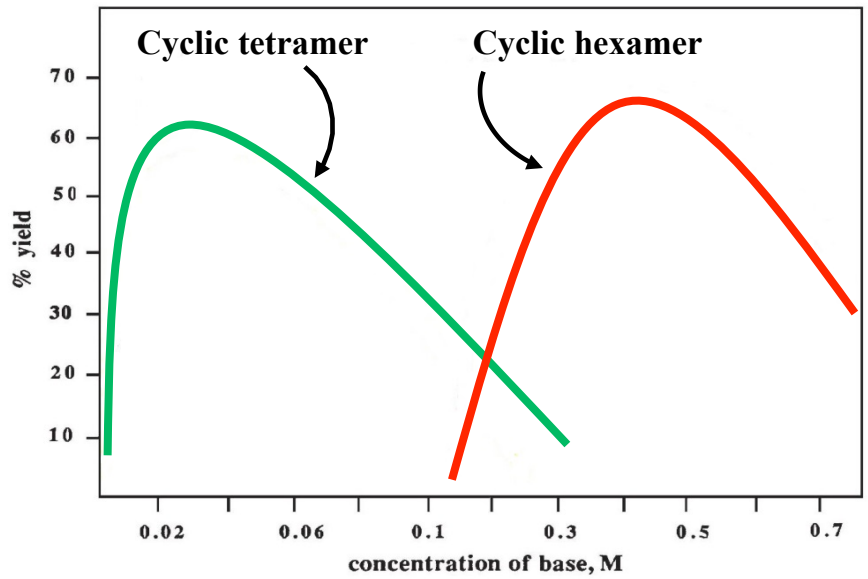


Figure 11 – Effect of base concentration in the formation of *p-tert*-butylcalix[4]arene.

Gutsche.[16] In this procedure, named by Gutsche "*Modified Zinke-Conforth Procedure*", *p-tert*-butylphenol and formaldehyde react in presence of small amounts of NaOH at 110-120°C. This procedure leads to a final yield higher than 60%. The optimum amount of NaOH, to maximise the yield of the *p-tert*-butylcalix[4]arene, is 0.03-0.04 equivalents of base as illustrated in *Figure 11*. The *p-tert*-butylcalix[6]arene becomes prevalent, or even the only product, at higher concentration of base with the same conditions (yield = 65%).

The amount of the base influences the final outcome of the reaction mostly, but sometimes also the cation, that accompanies the anion, has a little effect on the formation of the calixarene.[17] In general, using *p-tert*-butylphenol as starting material, lithium hydroxide is considered a worst base for the synthesis of calixarenes while sodium hydroxide gives higher yields of the *p-tert*-butylcalix[8]arene in the so called "*Modified Petrolite Procedure*"[18] and potassium hydroxide and cesium hydroxide tend to give higher yields of the cyclic hexamer in the "*Standard Petrolite Procedure*".[19]

All these procedures can be used to synthesised the "Major Calixarenes" (calix[4], -[6]-, -[8]arenes) easily and in very large scale. The cyclic pentamer and the cyclic eptamer, instead, are called "Minor Calixarenes" and are less available compared to the previous ones. Their synthesis is more difficult and in general the yields are very poor (about 10-20%).[20,21]

2.2.1 Mechanism of the Base-Induced Reaction

The mechanism of formation of calixarenes, at least after the first steps of oligomers formation, is still not well understood. After the acid-base reaction that generates the phenoxide, the initial step is the nucleophile attack of the phenoxide to the highly reactive carbonyl group of formaldehyde. Under heating conditions, the reaction continues and leads

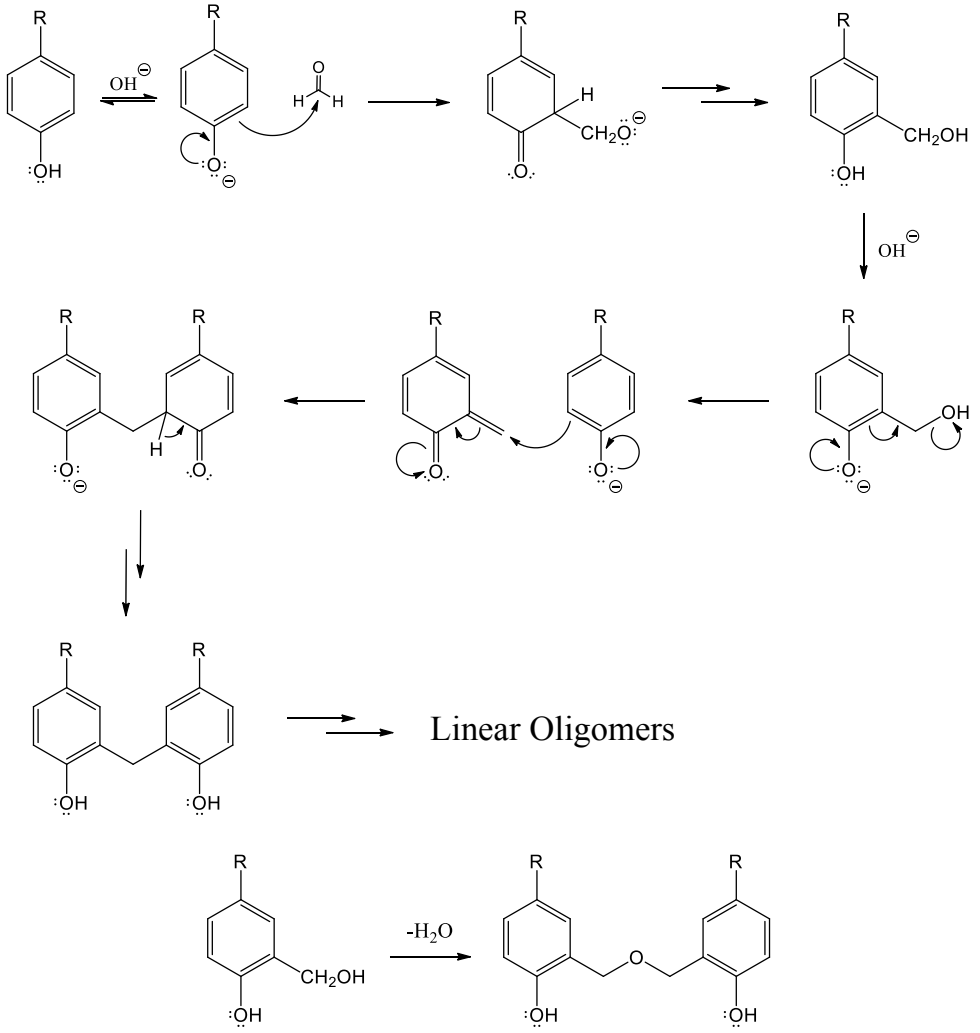


Figure 12 – On the Top: Mechanism of formation of linear oligomers. On the Bottom: Formation of dibenzyl ethers.

to the formation of diarylmethyl compounds, probably through an intermediate o-quinonemethyde (*Figure 12*). During this phase there are also minor reactions of dehydration of the hydroxymethylphenols that generate dibenzyl ethers. The final mixture from which calixarenes arise is composed by diphenylmethanes and dibenzyl ethers with different degrees of oligomerisation.

These compounds evolve then somehow to a cyclic calixarene but the exact pathway which leads to the formation of the different macrocycles is still unclear. Among the different theories, the most popular one was proposed by Gutsche and co-workers,[17] which suggested a mechanism based on hydrogen bonding considerations and reactions among oligomers.

An aggregate of a pair of mono- or bis-hydroxymethylated linear tetramers, called "hemicalix[8]arene" (*Figure 13*), forms by hydrogen-bonding. Extrusion of water and formaldehyde from the hemicalix[8]arene causes the formation of the calix[8]arene, that is the principal product of the *Modified Petrolite Procedure*. If solvent is changed from xylenes to the higher boiling diphenyl ether, there is first the formation of the calix[8]arene and, in the following step, the cyclic octamer is converted in the cyclic tetramer through a process called "molecular mitosis". Gutsche suggested that the cyclic octamer pinches together to form a conformer, having the shape of a 8, which then splits into a pair of cyclic tetramers. So the order of events for the formation of the calix[4]arene is postulated to be: monomer → linear tetramers → hemicalix[8]arene → calix[8]arene → calix[4]arene.

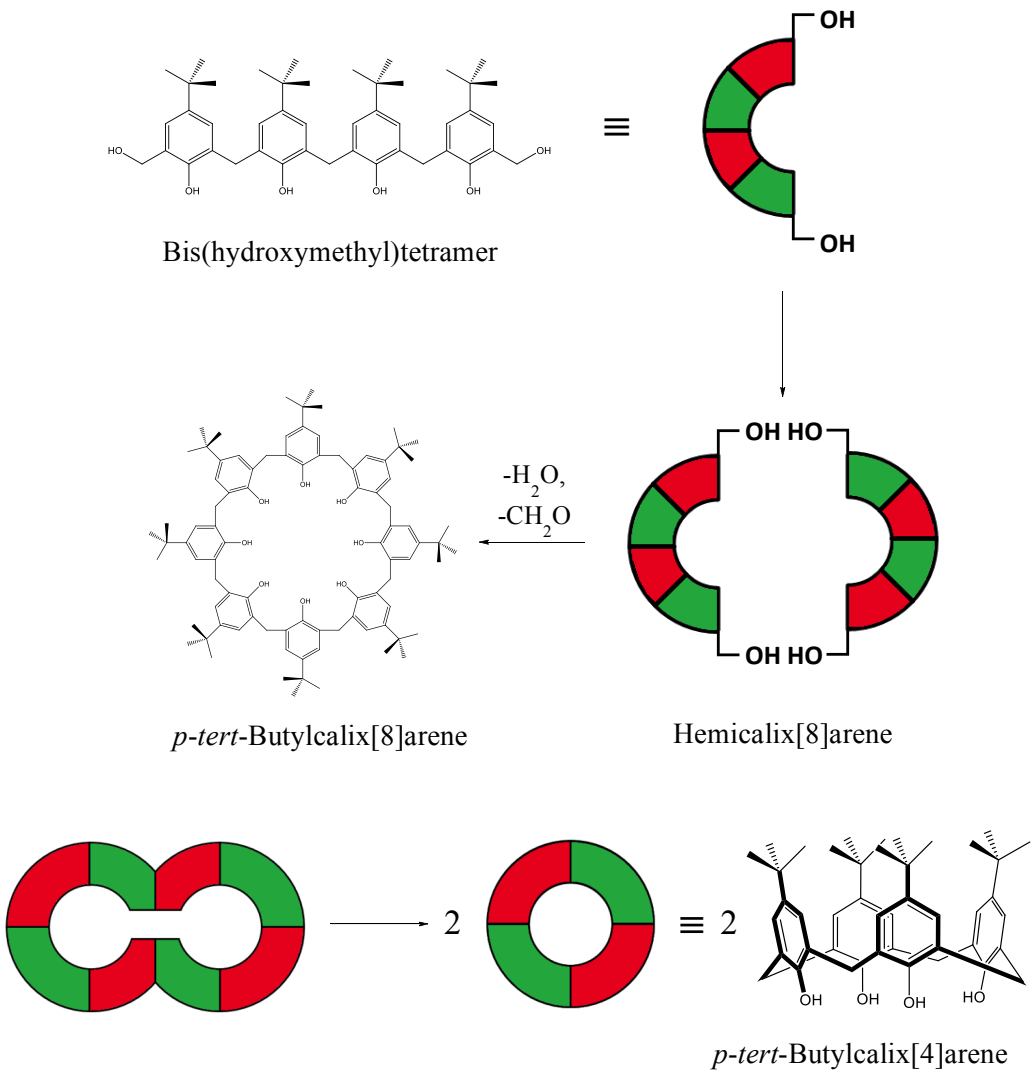


Figure 13 – On the Top: Mechanism of formation of *p-tert*-butylcalix[8]arene. On the Bottom: "Mitosis" of the *p-tert*-butylcalix[8]arene.

Unfortunately, there are little or no experimental evidences in support of these final steps which lead to the cyclisation, also because the reaction mixture becomes more and more complicated and rich of different products as soon as the reaction proceeds. However, it is generally accepted by all the different chemists working on these macrocycles, that in the formation of calixarenes from *p-tert*-butylphenol, the cyclic

octamer is the product of kinetic control (in presence of NaOH), the cyclic hexamer is the kinetic product under a template effect in presence of KOH, while the cyclic tetramer is the thermodynamic product (in presence of NaOH). Also, it is still quite puzzling, why these syntheses give extremely high yields of even-number calixarenes while odd-numbered ones are extremely rare and difficult to be synthesised.

2.2.2 Synthesis of Other p-Substituted Calixarenes

The *p-tert*-butylphenol is the most used reagent for the synthesis of calixarenes thanks to the well-studied and established procedures for the kilo-scale preparation and isolation of pure calix[n]arenes (n = 4, 6, 8). However there are also others phenols that were used to give one or another of these cyclic compounds in reasonable yields.

A large body of literature investigated the synthesis of calixarenes from different phenols, mainly those carrying a highly branched *p*-alkyl substituent. In fact with most of other *p*-substituted phenols (n-alkyl, halogen or aromatic groups) the results are considerably less favorable. For example: 4-nitrophenol, 4-hydroxybenzoic acid, 4-hydroxyacetophenone, 1,4-dihydroxybenzene (hydroquinone), 4-phenoxyphenol, 4-hydroxybenzyl alcohol and 4-cyanophenol do not lead to the formation of macrocycles.

Several studies show that is possible to synthesise and isolate calix[4]arene, calix[6]arene and calix[8]arene only starting from branched *p*-alkylphenols such as *p-tert*-pentylphenol and *p-tert*-octylphenol,[22–24]

though the yields are moderate and the purification step is more tedious with respect to *p*-*tert*-butylphenol.

Instead *p*-phenylphenol gives a mixture containing the cyclic tetramer, hexamer, eptamer and octamer with different yields depending on the reaction conditions.[25] In literature there are also other kind of calixarenes synthesised from *p*-isopropylphenol,[17] *p*-(benzyloxy)phenol,[26] *p*-adamanthylphenol, *p*-cresol[27,28] and *p*-ethylphenol.[28]

However the attempts to synthesise calixarenes with long chains at the upper rim always gave very poor results.[29] Furthermore in reviewing the literature, no data was found on the synthesis of calixarenes that involves phenols with *long* and *branched* chains in para position. Regarding this issue, there is a lack of presence of these compounds that can be more soluble in very apolar solvents for special industrial applications.

2.3 Introduction of Functional Groups

The considerable interest about calixarenes derives from the excellent results obtained with their use in a large number of applications. This depends not only from their basket-like character, but also from the possibility to easily modify their chemical structure by the introduction of the desired functional groups onto their macrocycle structure. Using this approach, researchers have been able to modify calixarenes to confer new properties. Modified calixarenes have been employed in different fields such as the recognition of cations,[30] anions,[31] small neutral molecules[32] and bio-relevant macromolecules,[33] self-assembly systems,[34] nanoporous

materials,[35] catalysis,[36] chiral recognition[37] and controlled release of bioactive molecules.[38]

2.3.1 Functionalisation of the Lower Rim

The lower rim of calixarenes is already functionalised with hydroxy groups that are excellent sites to introduce new functional moieties.

Esterification of calixarenes was the earliest reaction to be studied, because leads to products more soluble and easier to work with. In general in presence of an excess of the acylating agent and of a strong base like NaH, the acylation of all the hydroxy groups of a calix[4]arene occurs, blocking the molecule in one of the possible conformations. Which conformer is produced depends by the calixarene, the acylating agent and by possible template effects exerted by the cation present and the solvents.[39] By using acid halides in the presence of bases weaker than NaH and by using limiting amounts of the esterifying reagent and/or by using bulky esterifying reagents it is often possible to obtain partially substituted calixarenes.

The larger calixarenes generally react very well with acetic anhydride in presence of sulfuric acid to give the hexacetate and the octacetate,[40] so as the treatment with a moderate excess of aroyl chlorides in presence of NaH leads to complete acylation, like in the case of the *p-tert*-butylcalix[8]arene.[41] With different conditions it is also possible to generate partially substituted compounds having, however, a great conformational mobility.[41–43]

The formation of ethers on the phenolic O atoms is another very important reaction in the chemistry of calixarenes. Starting from the simple calix[4]arene, the complete tetralkylation can be achieved by using an excess of the alkylating agent in presence of a strong base like NaH.[44] The final conformation of the tetra-ethers is dependent by the reaction conditions (base, temperature, solvent), a possible template effect of the cation of the base and to minor extent by the type of alkylating agent and the *p*-substituent of the calixarene.[45]

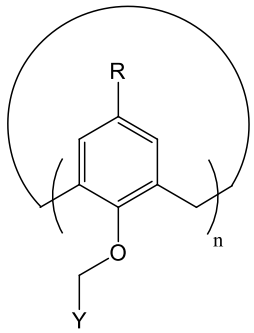
Furthermore, partial functionalisation at the hydroxy groups of the macrocycle has been extensively investigated. Changing the reaction conditions, it is possible to produce mono-ether, di-ether and tri-ether compounds. The monoalkylation of the calix[4]arene involve the use of stoichiometric amounts of alkylating agent and NaH in toluene[46] or NaOMe in acetonitrile.[47] For what is concerned with di-ethers, there are two structural isomers: the proximal (1,2) or distal (1,3) isomers. The synthesis of the dialkylated 1,2- and of the 1,3-products can be achieved using similar conditions to the monoethers but with different equivalents of the base and of the alkylating reagent. A strong base such as NaH in DMF or acetonitrile favors the 1,2-difunctionalisation,[48] while the use of K_2CO_3 in acetonitrile gives exclusively the 1,3-difunctionalised calix[4]arenes.[49,50]

There are also many studies regarding the trialkylation of calix[4]arenes. For example, the trimethylation of *p-tert*-butylcalix[4]arene can normally be obtained with a small excess of the alkylating agent in the presence of three equivalents of NaH.[46]

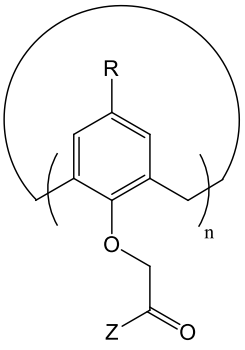
More complicated and considerably less selective are the reactions for the

partial functionalisation of larger calixarenes. Generally, mixtures of mono-alkylated and polyalkylated products are obtained, and the desired products can be isolated in moderate yields only rarely by crystallisation, being most of the times necessary a flash chromatography.[51–55] Among the larger calixarenes, the most popular reaction is the exhaustive alkylation of the lower rim and it is usually carried out using NaH in DMF or K_2CO_3 in acetone or acetonitrile.[56–59] The use of potassium carbonate in dry acetonitrile is an efficient method but requires more reactive electrophiles and longer reaction times. Due to the larger dimension of the cycles, in general the complete alkylation of the calix[6]- or calix[8]arene at the lower rim leads to conformationally mobile derivatives.

Esterification and etherification can be also used to introduce new functional groups onto the calixarene through the adoption of appropriately difunctionalised reagents (*Figure 14*). There are different kinds of these reagents, but alkylating reagents with formula $X(CH_2)_nY$ are widely used. In general X is a good leaving group such as -Br, -Cl or Tosyl, while Y is the new function to be introduced. A well-kwon example is the formation of allyl ethers[60] and propargyl ethers,[61,62] using respectively $BrCH_2CH{=}CH_2$ and $BrCH_2C{\equiv}CH$.



a) Y = $CH{=}CH_2$
b) Y = $C{\equiv}CH$
c) Y = CH_2CH_2OH
d) Y = $CH_2CH_2CH_2NH_2$
e) Y = 



a) Z = OR'
b) Z = NR'_2
c) Z = R'
d) Z = OH
e) Z = Cl

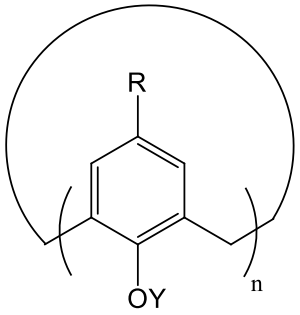
Figure 14 – Calixarenes with different functions at the lower rim.

Anyway the most used reagents are α-halo acetates/ketones or their derivatives with a structural formula equals to XCH_2COZ. With such compounds it is possible to introduce different types of esters,[56,63] amides[64] and ketones.[56] These moieties can be easily converted to a wide variety of other functional groups using standard functional groups transformation procedures.

2.3.2 Functionalisation of the Upper Rim

Quite favorably the phenols that give the higher yields in the synthesis of calixarenes are those having tertiary alkyl para-substituents that can be easily removed by a reverse Friedel-Craft reaction. Moreover the rate of the reaction of de-*tert*-butylation is strongly influenced by the presence of substituents on the lower rim, thus allowing to selectively remove the alkyl groups in para positions of phenols having a free OH at the lower rim.[49] The removal of the alkyl unit has a significant synthetic impact because it makes possible a variety of reactions for the introduction of functional groups on the upper rim mainly by electrophilic aromatic substitution. This allowed to introduce several groups such as halogens, $-NO_2$, $-SO_3H$, formyl, azo etc….

Alternatively the nitro group can be introduce via the so-called "ipso" nitration, proposed by Reinhoudt and coworkers,[65] that implies the direct displacement of the *tert*-butyl group. The reaction also in this case is influenced by the substituents on the lower rim, however it has the advantage that the removal of the *tert*-butyl groups in a separate step is not necessary. The nitrocalixarenes are very important intermediates in



a) R = NO_2

b) R = NH_2

c) R = SO_3H

d) R = CH_2Cl

e) R = COOH

f) R = CH_2OH

Figure 15 – Calixarenes with different functions at the upper rim.

the chemistry of these macrocycles because they can be interconverted in other functional groups, usually through their reduction to amines by using H_2 or NH_2NH_2 in presence of a metal catalyst.[66,67]

The CH_2Cl is another moiety that can be easily introduced thanks to the chloromethylation reaction.[68] It is a rather promising group because can easily react with nucleophiles for further modification.[69]

The formylation reaction, instead, inserts at the upper rim the formyl groups that are extremely useful thanks to their ease of conversion to various other different functional groups, such as carboxylic acids,[49] alcohols,[49] imine, amine and azomethines[70] and to alkenes via the Wittig reaction.[71,72]

2.4 Industrial Applications of Calixarenes

In the last years there was an increasing interest towards these macrocycles from industry, for several reasons.

Calixarenes are easily synthesised in simple one-pot procedures even in 1,000 kilo scales. Large amounts are available from rather inexpensive and readily available starting materials. They form a series of well-defined cyclic oligomers. The size of the cavity can be easily tuned according to the need and the requirements of different guests. They are also easily amenable to chemical modification. So starting from the parent compounds is possible to obtain a great amount of different derivatives with improved or special abilities.

The actual potential industrial application of calixarenes is related mostly to their power to separate metal ion and this ability was developed by synthesising special derivatives.[73] Additionally, they possess interesting properties such as high melting points, high thermal and chemical stability, low solubility in many solvents and low toxicity. All these peculiarities make calixarenes attractive subjects for special purposes.

Calixarenes are involved in many patents, and some of these led to significant special industrial applications. The most important fields in which calixarenes have been studied are: the recovery of cesium,[73] the recovery of uranium,[74] the selective complexation of metal cations,[75,76] as stabilisers for organic polymers,[77,78] as accelerators for instant adhesives,[79,80] and the separation of neutral organic molecules[81,82] or as phase transfer agents.[83]

Moreover, they were used also as demulsifiers of the crude oil. In fact when it comes out from the ground, the crude oil is mixed with water in an emulsion difficult to break. In the late seventies, the Petrolite Corporation in Missouri filed some patents for making cyclic phenol-formaldehyde oligomers that could be used as demulsifiers of the petroleum.[2]

2.4.1 Applications of Calixarenes in the field of Lubricants

In this work it is described the development and the study of new additives for lubricants based on calixarenes. The two main topics are Viscosity Index Improvers and Detergents.

In the literature and among patents there are no examples of calixarenes used for the preparation of Viscosity Index Improvers (VIIs). The benefit of these macrocycles in the production of VIIs is related to their well-defined structure and molecular weight, that lead to very narrow polydispersity: a crucial point in the design of novel classes of additives.

For what concerns detergents, both environmental issues with the need to lower emission of SO_x and the problem of sulfur poisoning of catalytic converters, have led to the increasingly important demand of sulfur-free detergents. Therefore there is a rush towards the development of novel detergents different from classical sulfonate (alkyl aryl sulfonic acid salts) and from the phenate (alkyl phenols *ortho*-linked by a sulfur bridge). Calixarenes have been proposed as novel sulfur-free surfactants for the synthesis of overbased detergents. Calixarenes with unprecedented

lipophilicity and compatibility with mineral/synthetic base-oil have been synthesised and studied to reach this goal.[84–86]

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Chapter 3

Calixarene-based Star Polymers as Viscosity Index Improvers

3.1 Introduction

The synthesis of novel multi-arm radial polymers has become of growing practical and theoretical interest for a large variety of industries. Such polymers are, in fact, now considered by many to be the cutting edge of viscosity index modifiers and oil additives.

The advantage of a structure with many arms is easy to explain. Take into account two species with the same molecular weight, one composed by single linear chain, the other one by many chains of lower length. At the beginning both of them will increase the viscosity of the oil nearly in the same way, however, when the oil is subject to the mechanical stress, the linear structure will be affected in a larger way from the "Shearing Effects". As explained in section *1.2.2*, a long chain has higher probability

to be broken and to lead to two molecules with a considerable lower molecular weight with respect to the weight of the original one. As a consequence a remarkable drop of the viscosity of the oil will be observed. By contrast, a multi arm structure with the same molecular weight will be provided of polymeric chains shorter and so it will be less affected by degradations due to shearing effects. Shorter chains, in fact, have fewer probability to be broken and, moreover, a potential break of one chain will cause the loss of only a rather small structure, as illustrated in *Figure 16*. This will end up in a substantial conservation of the overall structure and weight of the multi-branched macromolecule thus resulting in a thickening power lasting for a longer time and improving the quality of the oil.

Among the most promising polymeric structures in this sector, there are the Star Polymers. Star Polymers represent a broad class of branched

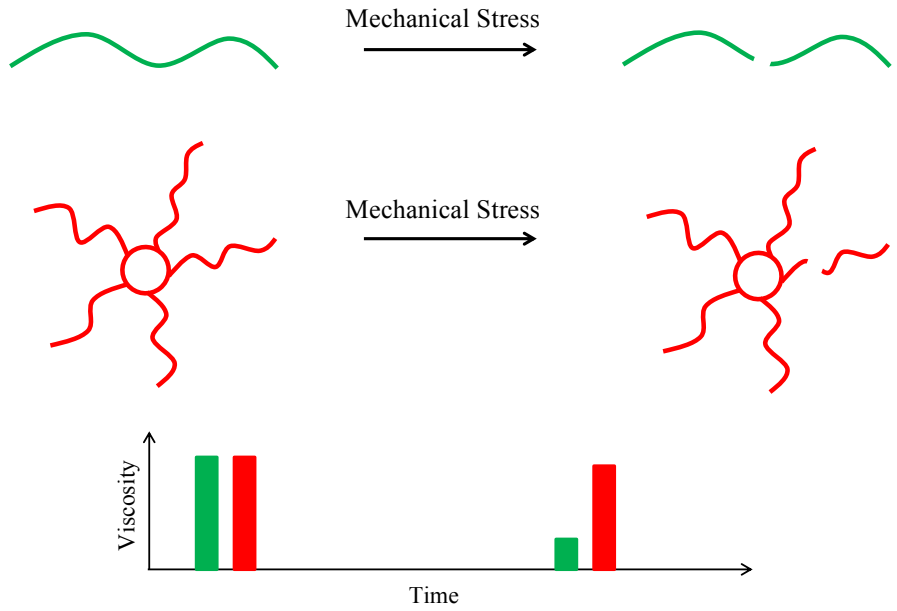


Figure 16 – Effects of the mechanical stress onto two different macromolecular structures.

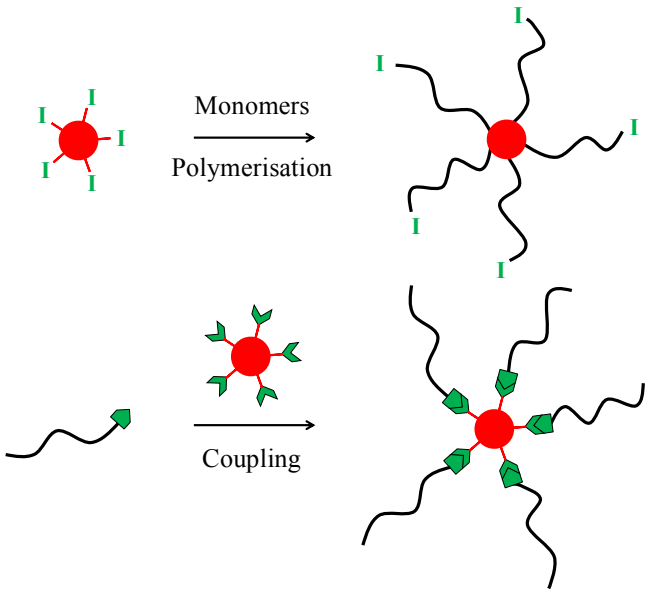


Figure 17 – On the top: Core-first approach. On the bottom: Arm-first approach.

macromolecular architectures with linear "*arms*" radiating from a central branching structure, typically referred to as the "*core*". The approaches used to synthesise Star Polymers are basically two: the "core first" and the "arm-first".[1]

The core-first approach employs a pre-synthesised multifunctional initiator (the *core*) to form star polymers. The arms grow from the core thanks to monomers present in solution that react with the growing chains. In contrast, in the arm-first approach, the arms are pre-formed even as block copolymers and star polymers are synthesised via coupling reaction between these arms and a properly functionalised core (*Figure 17*).

One of the most appealing aspects of the core first approach are the excellent yields that can be obtained; moreover, the pure star polymers can be easily isolated from the crude reaction, containing unreacted monomers, through simple operations such as precipitation. However, there are also a lot of limitations to this approach. The final product of the

"core first" approach generally has a low number of arms, arms show a shorter length and moreover the synthesis of a stable multifunctional initiator core is a critical issue. A further drawback is that the polymeric arms of the synthesised stars cannot be directly characterised, so indirect methods must be employed to determine their length or molecular weight, such as, for example, the isolation of the polymeric arms after cleavage. In addition to these problems, when the controlled polymerisation is taking place to produce the star polymers, special precautions should be taken to prevent side reactions that may lead to star-to-star coupling, coupling between arms on the same star and termination of the growing arm polymers, since all these events results in star products with rather wide molecular weight distributions.

In contrast to the core-first approach, in the arm-first approach the linear arms are firstly synthesised and characterised before their conjugation to the central core. This end up in a high level of control on the star polymer structure. After the coupling reaction between the linear arms and the core, sometimes a final purification step is necessary to separate the star polymer from the unreacted chains. However the final product has usually a large number of arms and a high molecular weight that cannot be reached through the core first approach.

3.2 Aims of Research

In this chapter, it will be reported the efforts to use calixarenes as multifunctional cores for the synthesis of star polymers via the arm-first approach.

Calixarenes derivatives could potentially improve the properties of star polymers as Viscosity Index Improvers (VII) generating structures with high and well defined number of branches and with very low polydispersity.

The ideal candidate for this purpose are the calix[8]arenes because they have a large number of sites that can be functionalised with reactive groups able to be coupled with the polymeric arms. Moreover, as explained in *Chapter 2*, the calix[8]arene derivatives are conformationally mobile. So, this feature can reduce the steric hindrance around the core during the coupling step with the linear polymers and can maximise the conversion into star.

The polymerisation techniques chosen to synthesise the arms are two: the living anionic polymerisation and the radical controlled polymerisation. For these reasons the calixarene derivatives were functionalised with two kinds of moieties: reactive groups, such as esters, epoxides and alkyl halides, able to react with living anionic alkyl chains and groups such as acrylates able to react with radicals.

3.3 Calixarene-based Star Polymers using Living Anionic Polymerisation: Previous Work

Previous work carried out in our research unit,[2] explored the use of different reactive groups on the *p-tert*-butylcalix[8]arene platform to find the appropriate functionality able to react with the anionic polymer chain grown using a living anionic polymerisation.

Different groups were studied such as alkyl halides, alkenes and esters. Among them the most promising ones were shown to be esters with no hydrogens in α position to the carbonyl groups. In fact, if hydrogens in alfa position are present, they are sufficiently acid to be extracted in an acid-base reaction by the anionic polymer chains preventing the addition of the anion to the carbonyl groups by quenching the carboanion species. Moreover, each of the ester groups allows the addition of two equivalent of anionic linear polymers. In the first step, in fact, the displacement of the alkoxide residue takes place with the formation of a ketone group which then reacts, even faster, with a second anionic chain to give a

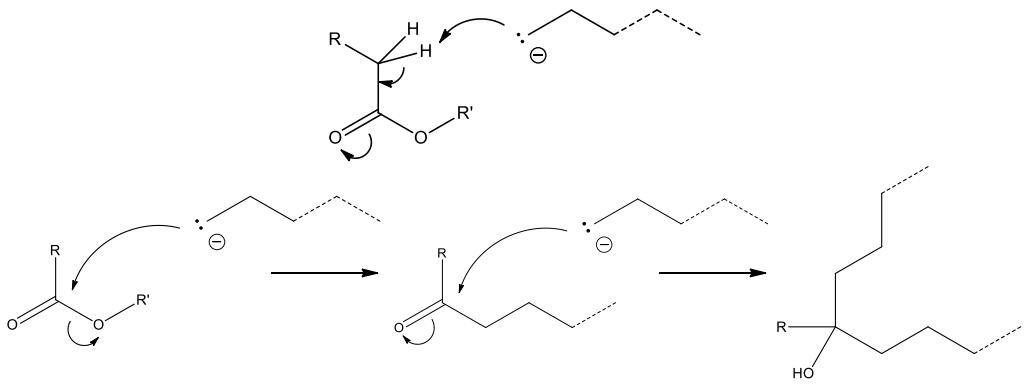
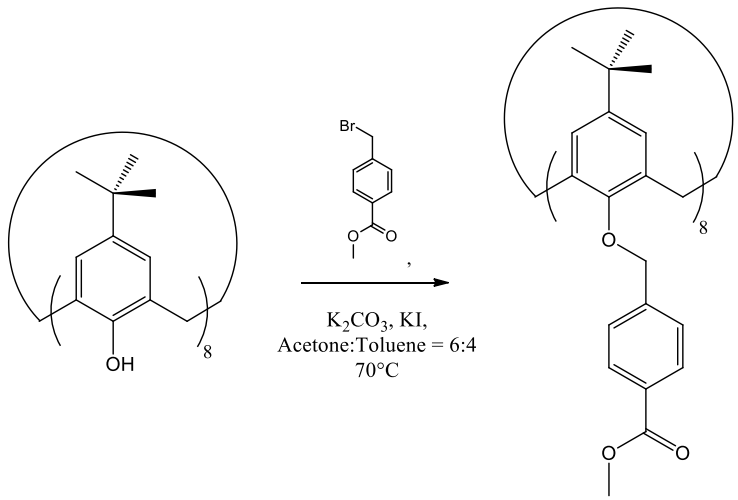


Figure 18 – On the top: Reaction of anionic linear polymers with hydrogen atoms in α to carbonyl groups. On the bottom: General reaction of anionic linear polymers with esters.

tertiary alcohol. This peculiarity makes the ester group rather appealing because it potentially allows to link two polymer chains for each arms of units of the calix[8]arene core thus yielding up to 16 arms in the final star polymer.

As a relevant results, the previous research activity produced the calix[8]arene derivative **2** in *Figure 19*. Product **2** was synthesised by reaction of the *p-tert*-butylcalix[8]arene with methyl *p*-(bromomethyl)benzoate. The reaction was carried out in the presence of potassium carbonate and of a catalytic amount of potassium iodide with acetone and toluene as solvents. After two days at 70°C the reaction affords the product in good yields as confirmed by NMR and mass spectroscopy.

After the synthesis of the calixarene derivative **2**, the study of its reactivity towards living anionic polymer chains was also carried out. It was chosen a simple reactant such as *n*-butyllithium to model the reactivity of the



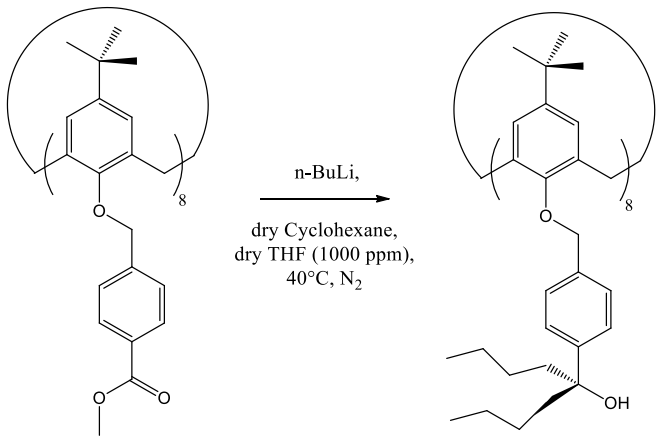
1 **2**

Figure 19 – Synthesis of the calixarene derivative **2**.

anionic polymer chains towards **2**. The use of *n*-butyllitium, in fact, allows to overcome the possible low reactivity of carbanionic polymer chains due to their steric hindrance and to favor the formation of products of low molecular weight easier to be analysed and characterised.

Derivative **2** was solubilised in 10 ml of dry cyclohexane containing up to 1000 ppm of dry THF (to favor solubility and increase reactivity), the same solvent mixture used in the living anionic polymerisation carried out in an industrial plant. This solution was heated to 40°C under inert atmosphere and then *n*-BuLi was added to the solution (2 equivalents for each ester group) and the reaction mixture was stirred for about 40 minutes. At the end the final analyses showed that all the esters groups reacted with the two equivalents of *n*-BuLi leading to final product **3** (*Figure 20*).

For this reason, derivate **2** is an excellent candidate for the synthesis of star polymers by grafting living anionic polymer chains on the calixarene structure.



2 **3**

Figure 20 – Reaction of *n*-BuLi with **2**.

The preparation of the calixarene-based star polymers was carried out following the arm-first approach (*Figure 21*). The synthesis is divided into three steps. The first one is the synthesis of the living polymer chains obtained before the addition of the calixarene core unit.

The polymer chains used were block copolymers formed by 1,3-butadiene and styrene in ratio 9:1. These two monomers are rather frequent in many patents for the preparation of Viscosity Index Improvers. Butadiene is used because it is a cheap compound and because the reduction step, that will be illustrated later, is very efficient on this monomer. Instead styrene

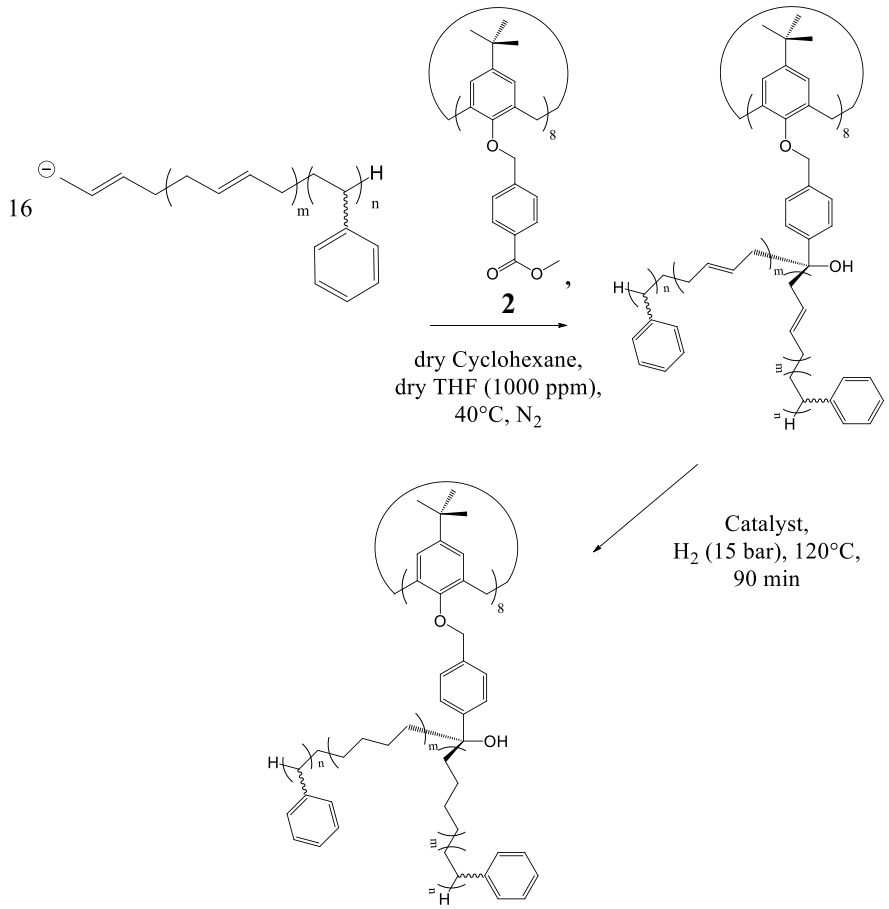


Figure 21 – Synthesis of the Calixarene-based Star Polymer.

is added because it gives dispersant properties to the final product by helping to keep in solution (in the oil) the so-called "*soot*" that is a by-product of combustion in diesel engines.

In details, styrene was added, in an inert atmosphere, to a mixture of dry cyclohexane and dry THF. The solution was heated at 40°C, then a solution of *n*-BuLi was added. Once styrene conversion was completed (about 20 minutes), butadiene was added to the solution to form the second block of the linear copolymer.

To this mixture of reactive arms was then added derivate **2** in a solution of dry THF by a dropping funnel (second step of the synthesis). The coupling reaction between the core and the arms takes place during this phase. After 45 minutes the reaction between the calixarene and the anionic polymer chains was finished and the mixture was subjected to a hydrogenation phase to remove the unsaturations of the arms of the star polymer. This step is necessary to increase the thermo-oxidative stability of the final product. The catalyst used for the hydrogenation process is a mixture of butylethylmagnesium in Heptane solution and cyclopentadienyl-titanium dichloride in cyclohexane solution. After the addition of the catalyst, the mixture was stirred under hydrogen pressure (15 bar) and maintained at 120°C for 90 minutes. At the end the mixture was moved into a stripping system, in which the solvents were removed under reduced pressure. The resulting granular product was dried in a vacuum oven.

Unfortunately the final analyses carried out by GPC-MALLS showed that the conversion into star polymer was not complete. In fact the product was composed by a 53% of star polymer and about 47% of unreacted linear

arms. The number of arms linked to core was, on the average, 12-13, a value still rather far from the theoretical one of 16. Steric hindrance could be a possible reason of this result. As soon as the different arms link to the central structure, the steric hindrance around the core increases and thus impairing the linkage of other chains to the central core. However, with these characteristics, the star polymer was not able to increase, as requested, the performances of the oil, so that it was required to try to carry out some purification with the aim to separate the star polymer from the linear arms.

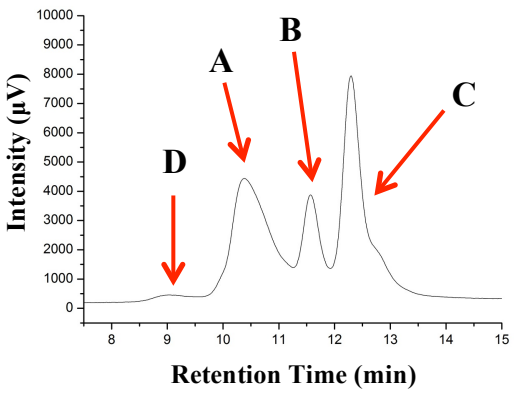
3.4 Work Developed in this Thesis for the Purification of the Star Polymer

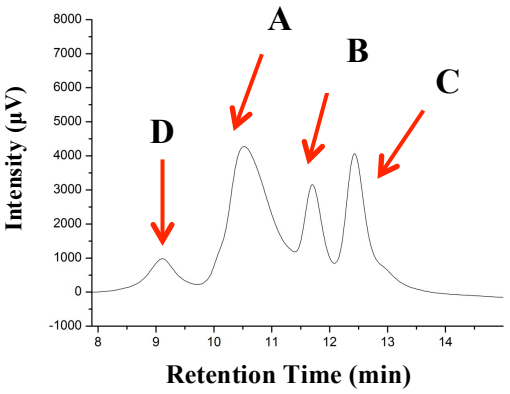
The purification of the star polymer from the unreacted linear arms was successfully achieved, during this thesis work, by fractional precipitation following a procedure reported in the literature.[3] It has to be noted that purification of polymers by fractional precipitation is a quite challenging task, consisting in various methods suitable for segmentation of macromolecules according to their size and to the their different solubility. The experimental processes of fractionation can be divided into two groups: preparative methods, in which fractions with different molar mass are collected leading to a segmentation of the polymer, and analytical methods, in which a distribution curve is determined on the basis of change observations of a physical property of polymer that is dependent on molar mass of fractions and thus accompanies the

segmentation, for example GPC. In this case it was used a *Gradual Fraction Precipitation* that belongs to the methods of the first group. In this method a precipitant is added gradually to a solution of the polymers and the first separated fraction in general contains the polymer with the biggest molar mass.

According to this technique, the crude product was dissolved in toluene then, under moderate stirring, it was added methanol dropwise until the solution became turbid. At this point the solution was heated at 40°C until everything dissolves again. The mixture was subsequently cooled to room temperature and let it rest for several hours. The precipitate, assumed to be enriched in star polymer, was then separated by simple decantation and it was dried under vacuum at room temperature. At the end three samples, the crude product, the separated fraction and the mother liquor, were sent to the University of Pisa to the research group of the Prof. Ciardelli and Pucci, who analysed them through a Gel Permeation Chromatography.

The two graphs in *Figure 22* illustrate the composition of the crude product (on the left) and of the precipitate (on the right) after the purification. The most important peaks are A and C: peak A belongs to the star polymer while peak C is given by the linear arms not reacted. In the graph there are also other two peaks: peak B is due to the coupling reaction between two anion polymers, a well-known side reaction. Peak D belongs to a species with a very high molecular weight. Although a convincing explanation on the origin of this species could not be corroborated by experimental data, it might be that it origins from a side reaction that takes place during the synthesis such as a oligomerisation of the growing calixarene star polymer. In any case, as can be noted from





	Peak A	Peak B	Peak C	Peak D
Mn	234600	124800	62700	888000
Mw	295000	130000	77700	1038000
Id	1.258	1.041	1.238	1.169
Area (%)	39	14	44	3

	Peak A	Peak B	Peak C	Peak D
Mn	218800	81600	37800	903100
Mw	240800	84000	40000	949100
Id	1.100	1.028	1.047	1.051
Area (%)	50	19	27	4

Figure 22 – On the left: GPC analyses of the crude product. On The right: GPC analyses of the precipitate.

Figure 22 left, in the crude reaction, compound D is present in a rather tiny amount while its presence appears much more important after the precipitation, probably because is one of the species that more easily precipitates.

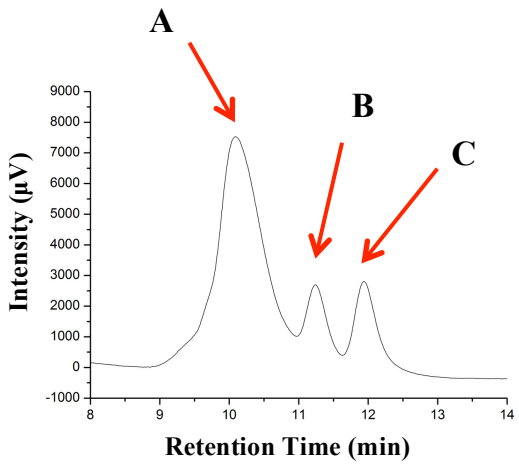
However, the results in *Figure 22* underline an important finding, the precipitate is consistently enriched by the star polymer. In fact the area of the peak A (Star Polymer) increased from 39% to 50%. Moreover, to confirm this data, the results of the GPC analysis of the mother liquor showed that they are composed mainly by linear arms not reacted.

Considering that the separation of these two species is really hard because of the rather similar chemical nature, the precipitation gives rather good

results. For this reason the study of the purification was continued modifying the solvents used. In particular different solvent combination were studied especially with the aim to substitute methanol because of the very low solubility of both star polymer and linear arms.

Different pairs of solvents and different conditions were investigated: toluene-methanol, toluene-methanol (without heating), cyclohexane-acetone and cyclohexane-isopropanol. Moreover, every precipitation was repeated on the precipitate for three succeeding times to check if a higher number of fractionations could improve the final purity of star polymer.

Again, samples (precipitate and surnatant) of every step of purification and for every solvent couples, were sent to Pisa for the GPC analyses. The final outcome highlights that cyclohexane-isopropanol is the best couple of solvent for this fractionation. As reported in *Figure 23*, after two precipitations the percentage of star polymer increased to about 70%, while after the third precipitation no important changes in the percentage of the star polymer were observed. So two precipitations have been



	Peak A	Peak B	Peak C
Mn	334000	127000	64000
Mw	378800	131000	65000
Id	1.130	1.029	1.020
Area (%)	70	14	16

Figure 23 – GPC analyses of the sample after two precipitation with cyclohexane/isopropanol.

considered sufficiently to obtain an enriched sample of star polymer.
The fractionation of this star polymer was repeated on a large scale of roughly 30 g of purified sample to have the possibility to test the real potentials of the calixarene-based star polymer.

3.4.1 Test on the purified Star Polymer

In order to test the properties as VII, solutions at different concentrations of the purified star polymer in base oil were prepared. Other solutions in base oil of other samples were prepared, dissolving the non-purified star polymer and other two viscosity index improvers, used as reference, having a star polymer structure with polydivinylbenzene core and constituted by block copolymers of styrene and butadiene. These solutions were used to compare the data before and after the purification and to compare calixarene-based star polymers with star polymers having a more classical core.
The base oil used was SN 150S, a base oil of the group I. Solubilisation was performed by heating the base oil at about 120°C, then the polymer was added and the mixture was stirred until complete solubilisation.
The thickening power was determined on the solutions at 1% of Viscosity Index Improver in base oil.
The Thickening Power is calculated as the difference between the kinematic viscosity value at 100°C of the solution of base oil containing 1% in weight of the Viscosity Modifier (VM) and the kinematic viscosity value at 100°C of the base oil. The higher is this value, better are the performances of the viscosity index improver.

Instead, for the determination of the Shear Stability Index (SSI) the solutions of the viscosity modifiers in base oil were prepared at a concentration in such a way to obtain kinematic viscosities at 100°C very similar (same thickening power).

The concentrations of the solutions of the star polymers in SN 150S were:

- Calix Star before purification: 2.1% w/w;
- Calix Star after purification: 1.5% w/w;
- Star VII (A): 1.35% w/w;
- Star VII (B): 1.64% w/w.

The Shear Stability Index is equal to the ratio between the loss of viscosity of the oil after the shear test and the difference between the viscosity of the oil before the shear test and the viscosity of the base oil, multiplied for 100. In this case, lower is the final value, higher the stability of the product.

Table 2 shows the results of the thickening power and of the shear stability index for the purified Calixarene Star Polymer and for the other solutions of Star Polymers. What can be clearly ascertained from the data in the table is that there is an important growth of the thickening power of the star polymer after the purification (+40%), with the value increasing from 3.2 to 4.5. This is a promising thickening power that compares very well with those of the two polydivinylbenzene core products reported in the last two columns. Also the shear stability index present quite promising values. Although there is a small worsening of SSI from 11 to 13 upon purification (a change however not too significant) the class of calixarene-based VII ranks in between the values of Star A and Star B. So, in summary, compared to Star A polymer, the calixarene-based VIIs are

	Calix Star Before Purification	Calix Star After Purification	STAR VII (A)	STAR VII (B)
Thickening Power (cSt)	3.2	4.5	5.4	4.1
SSI	11.0	13.0	20.1	7.2

$$\text{Shear Stability Index (S.S.I.)} = \frac{\text{Viscosity Loss}}{\text{Polymeric Viscosity Thickening Before Shear}} \times 100$$

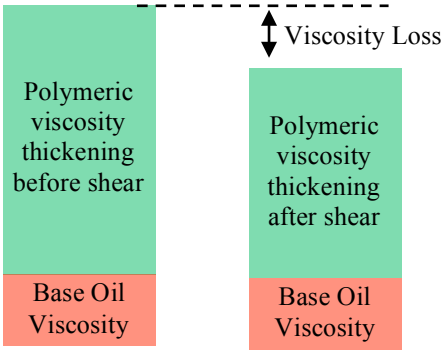


Table 2 – Comparison between calixarene-base Star Polymer and other VII in base oil.

fairly better for the shear stability but slightly worse in terms of thickening power.

The calixarene-based star polymers were also used to prepare complete lubricant formulations. To a mixture of base oils, a solution of star polymer in base oil at a concentration as reported in line 1 of *Table 3* was added. Subsequently, an additive package containing dispersants, detergents, antioxidants and antiwear additives was added in order to generate a classical formulation for a multigrade oil able to work in a great range of temperatures. The four compositions were prepared in such a way that their kinematic viscosities at 100°C were very similar (first two lines of *Table 3*). The final composition of the four formulations was: 79% of base oil, 14% of additive package and 7% of viscosity index improver.

The lubricants were characterised by determining the following parameters: kinematic viscosity at 100°C, kinematic viscosity at 40°C, viscosity CCS (Cold Cranking Simulator) at -25°C and the percentage of viscosity loss by depolymerisation (*Table 3*).

A very important parameter is the viscosity CCS at -25°C. CCS is the low-temperature dynamic viscosity that simulates the engine start up at low temperature. At low temperature the lubricant should not be too much viscous in order to avoid problems during the starting of the engine. This value must be under 7000. Before the purification, the viscosity CCS was more than 7500 a very high value for this parameter, but after the purification there was a fairly decrease to about 7000, being a good improvement.

The viscosity loss by depolymerisation is the result of a shear test (CEC

	Calix Star Before Purification	**Calix Star After Purification**	**STAR VII (A)**	**STAR VII (B)**
Star Polymer amount in the Viscosity Modifier additive (% weight)	21.00	15.00	13.50	16.40
Polymer amount in the formulation (% weight)	1.47	1.05	0.95	1.15
Kinematic Viscosity @ 100°C (cSt)	13.87	13.93	13.58	13.78
Kinematic Viscosity @ 40°C (cSt)	93.32	89.08	91.16	92.26
Viscosity CCS @ -25°C (cP)	7554	7039	6373	6965
Viscosity loss by depolym. %	2.2	5.0	10.0	2.0

Table 3 – Comparison between calixarene-base Star Polymer and other VIIs in lubricant formulation.

L14-A-88). The lubricant oil contanining the viscosity index improver is pumped thirty times under pressure through a Bosch injector in an apparatus (Bosch injector rig). The results of the test are the two kinematic viscosity values of the oil at 100°C before and after the shear test. Using these results, it was therefore possible to calculate the percentage of viscosity loss.

The loss of viscosity by depolymerisation of our purified star polymer has a value of 5 and this means that the product has a very good stability to shear stress. These data are very good and comparable to those of STAR VII-B and significantly better than those of STAR VII-A.

3.5 Improving the stability of ester arms present on calixarene cores

The previous section showed that it is possible to obtain star polymers using a calixarene core and that these products have very promising properties as VII. These results encouraged us to continue on this field trying to remove the decoupling problems observed with calixarene esters bearing a benzyl ether bond.

The incomplete conversion into star polymers observed with benzyl ethers (O-CH_2PhCOOEt substituents at the lower rim) was, in fact, referred to two main reasons: the steric hindrance that increases around the calixarene core as far as the number of arms attached increases and the lability of the benzyl ether bonds present in the structure of derivative **2** during the final hydrogenation reaction. It is well known that benzylic

ethers can be cleaved by hydrogenation, so during the second step, necessary to remove the unsaturation in the branches of the star polymer, it is possible that some arms decouple from the structure. In order to prevent these drawbacks new synthetic strategies were used. It was therefore decided to: i) introduce a spacer between the core and the functional groups, to reduce the steric hindrance that arises upon coupling of the arms to the central core; ii) remove the benzyl ether function in the final core by using a different reaction for the introduction of the ester groups. At the beginning the ethyl benzoate moiety, that showed excellent reactivity with the living anion chains and with the model butyl lithium compound, was kept constant. In order to first check this new synthetic methodology on a simpler monovalent structure, we tuned the reactions conditions on *p-tert*-butylphenol. The first modification studied involved the use of the Sonogashira reaction.[4] This should bring to a very stable linker between the calixarene and the benzoate. Moreover, the presence of a triple bond should not be a problem in the final star polymers since the final hydrogenation programmed to remove the alkene bonds will remove also this alkyne bond.

In *Figure 24* the Sonogashira approach for the introduction of the ethyl benzoate moiety on the simple phenol is illustrated. This new approach envisage the functionalisation of the hydroxy group of the phenol with a propargyl group. The resulting alkyne **4** should then be coupled with the commercially available aryl bromide **5**, to give product **6**. The final product has no more a benzyl ether while there are two extra carbon atoms in the linker between the phenol and the ester group.

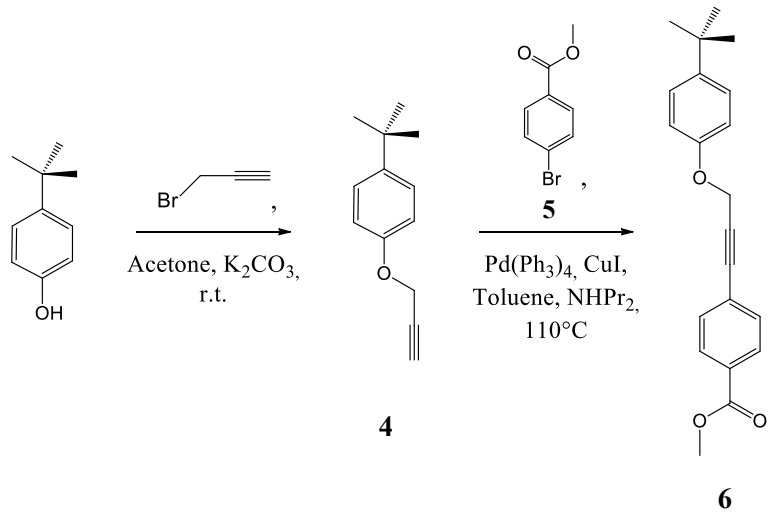


Figure 24 – Synthesis of derivative **6**.

The formation of the ether **4** was performed following the procedure already present in literature.[5] The reaction was carried out in the presence of potassium carbonate in acetone at room temperature with propargyl bromide. The alkylating reagent is an excellent electrophile, thus the reaction was completed in less than 10 hours. Product **4** was obtained as a crude and no further purifications were needed. Its formation was confirmed by ^{1}H NMR spectroscopy.

The next step was the Sonogashira reaction between **4** and an excess of methyl 4-bromobenzoate (**5**) to arrive to the final product, following procedures present in literature.[6,7] The reaction was catalysed by tetrakis(triphenylphosphine)palladium(0) in the presence of diisopropylamine, copper iodide and toluene as a solvent and it was heated at 110°C. After 24 hours the TLC analysis showed that derivative **4** was completely consumed and the reaction was stopped. The crude product was purified by flash chromatography in order to separate the derivative **6** from the unreacted methyl 4-bromobenzoate.

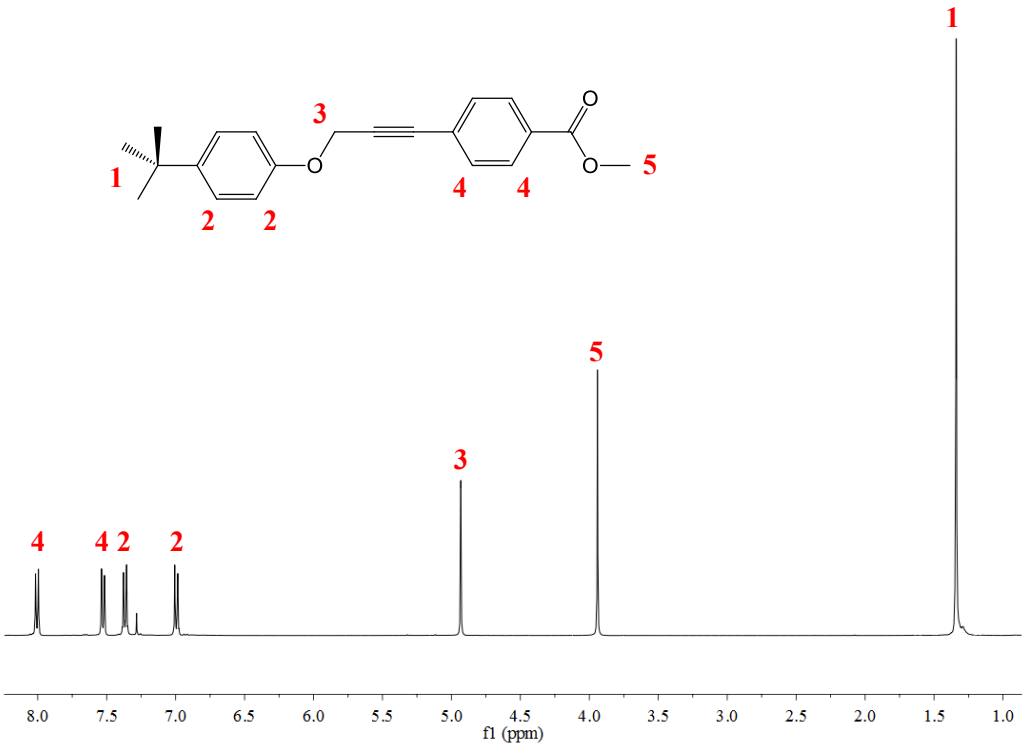


Figure 25 – ^{1}H NMR spectrum of compound **6** (400 MHz, $CDCl_3$, 25°C).

The successful outcome of the reaction was confirmed by the ^{1}H NMR spectrum in *Figure 25*. The new benzoate function was therefore successfully introduced in ether **4** as evidenced by the singlet at 3.94 ppm that belongs to the hydrogens of the methyl. The aromatic protons of the benzoate generate the two doublets at very low fields (> 7.5 ppm). Interestingly there are no traces of the signal of the hydrogen of the alkyne of **4** that in general resonates at about 3 ppm.

However the final yield of the reaction was only 11%, a result not satisfying considering the usually very high efficiency of the Sonogashira reaction and especially in view of its eight-fold repetition necessary when the reaction has to be transposed on the calix[8]arene. In order to improve this result, the reaction conditions were modified: different amines were

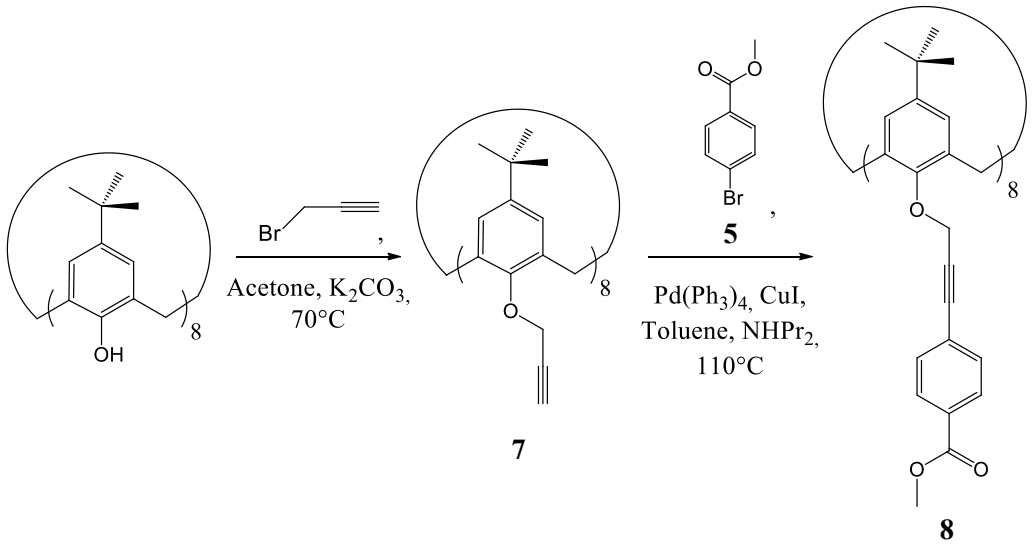


Figure 26 – Synthesis of the derivative **8**.

tested and other catalysts were used such as bis(triphenylphosphine) palladium(II) dichloride. In fact it is well-known that for the Sonogashira reaction catalysts of palladium (II) give better results, these being reduced in situ from palladium (II) to palladium (0). Despite these efforts the yield of product **6** was not considerably increased.

Anyway the new synthetic route was applied to the *p-tert*-butylcalix[8]arene hoping that, in any case, some compound could have been obtained. Similarly to **6**, the first propargylation reaction resulted in the complete functionalisation of the lower rim of the *p-tert*-butylcalix[8]arene. The employed conditions were the same, but this time the reaction was carried out at 70°C, being aware that reactions on calixarenes are usually slower than on simpler phenol models. Derivative **7** was purified simply through precipitation in ethyl acetate/methanol and it was isolated with a 94% yield.

In *Figure 27* the ^{1}H NMR spectrum of compound **7** is reported. At 4.23 ppm is present a doublet corresponding to the hydrogens of the

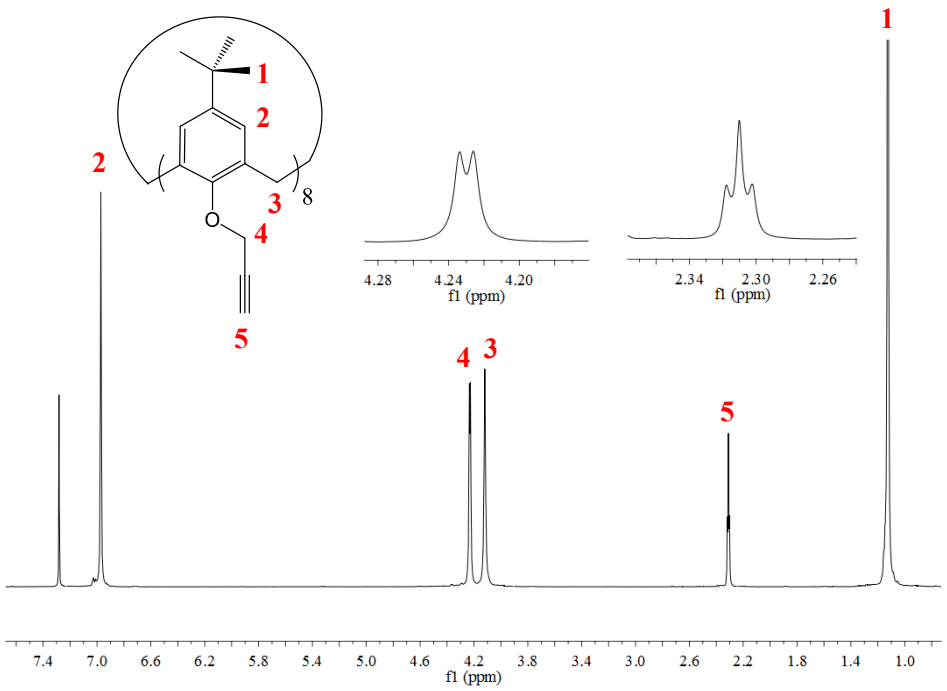


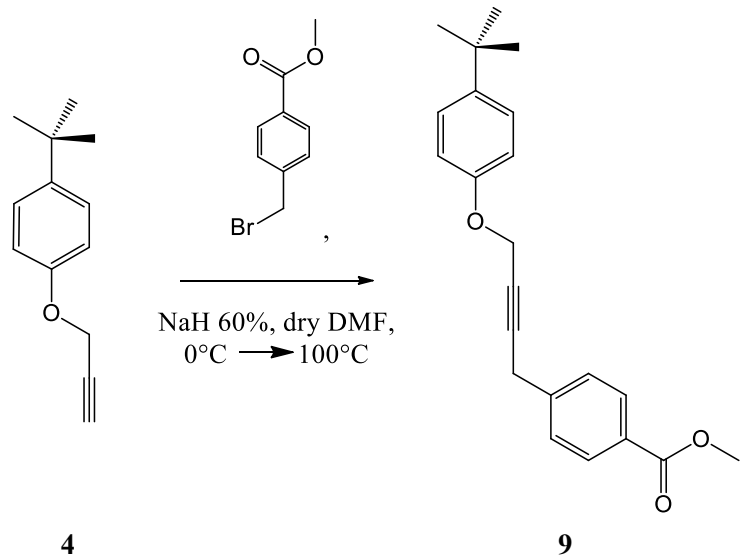
Figure 27 – ^{1}H NMR spectrum of compound **7** (300 MHz, $CDCl_3$, 25°C).

oxymethylene groups of the calix[8]arene, which is coupled with the triplet at 2.31 ppm belonging to the hydrogen of the terminal alkyne. The hydrogens of the methylene bridge, on the other hand, give rise to the singlet at 4.11 ppm indicating that, as expected, the calix[8]arene derivative is rapidly interconverting among different conformers (mobile conformation). Moreover, to further check the absence, even in small amounts, of partially functionalised intermediates in the final product, it was also recorded a mass spectrum with ESI(+) source. The spectrum showed only one peak of value 1623 m/z corresponding to the sodium adduct $[M+Na]^+$ of derivative **7**.

At this point the Sonogashira reaction was performed on **7** with the same conditions used for **4**. As observed previously for the monomer, the TLC analyses showed the complete consumption of **7** and the reaction was

quenched. After the work up, it was tried to isolate the product by simple precipitation through a 1:1 mixture of dichloromethane/methanol. The procedure afforded a great amount of a white solid that was separated and dried. However, thanks to the ^{1}H NMR spectrum, the white solid was identified as simple *p-tert*-butylcalix[8]arene. After a more careful research in literature,[8] it was evidenced that palladium catalyst can indeed cause the cleavage of the propargyl groups restoring the hydroxyl groups of the calix[8]arene. This last result clearly pointed out that the synthetic route suggested that uses the Sonogashira reaction could not be applied to our system. However, since product **7** can be synthesised in excellent yields, we though to exploit the propargyl group as nucleophile in a nucleophilic displacement reaction. For these reasons, monomer **4** was reacted with a stoichiometric amount of methyl *p*-(bromomethyl)benzoate in view of the obtainment of product **9** (*Figure 28*).

To test this new possibility monomer **4**, already synthesised, was dissolved in DMF. Then NaH was added carefully at 0°C and the mixture



4 **9**

Figure 28 – Synthesis of the derivative **9**.

was stirred for thirty minutes to favor the deprotonation of the alkyne. Then methyl *p*-(bromomethyl)benzoate was added in stoichiometric amount over a period of 20 minutes. After 24 hours, the TLC analysis showed the formation of a new species but also the presence of an unjustified large amount of the methyl *p*-(bromomethyl)benzoate. No propargyl ether **4** was, on the other hand, present. It was hypothesised that there was a side reaction that consumed product **4** avoiding the formation of derivative **9**. In order to confirm this hypothesis the reaction was quenched and the new species was separated by flash chromatography.

The ^{1}H NMR spectrum of the new compound was not related to compound **7**, so it was necessary to also acquire an ESI-MS spectrum to understand the structure of the main product. The spectrum, illustrated in

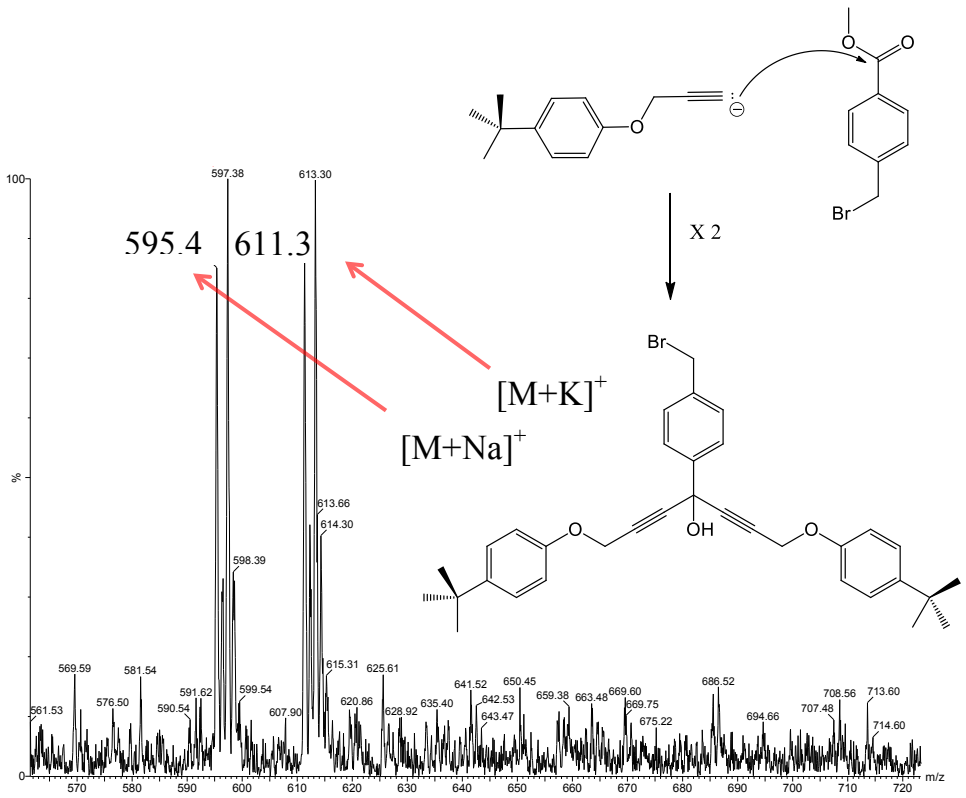


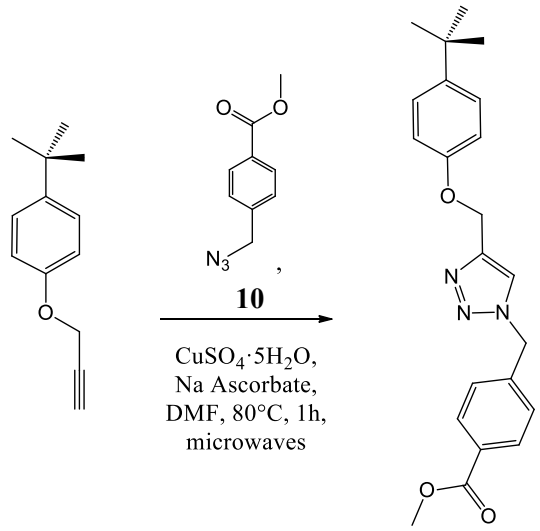
Figure 29 – ESI-MS spectrum of the side-product.

Figure 29, shows two groups of peaks. The group on the left has as first value of 595.4 m/z, instead the group on the right shows a value of 611.3 m/z. These two peaks have been attributed to the sodium adduct and the potassium adduct of the byproduct that is generated from the double attack of the alkyne on the ester group of the methyl *p*-(bromomethyl)benzoate. This suggestion could explain the excess of methyl *p*-(bromomethyl)benzoate that is indeed still present in the final mixture. In fact to form only one molecule of the byproduct two molecules of the alkyne are consumed leaving one equivalent of the methyl *p*-(bromomethyl)benzoate in solution. In conclusion the attack of the alkyne is much faster on the ester group compared to the benzyl halide thus avoiding the formation of the desired product.

Due to the problems underlined in the previous attempts, a new synthetic strategy was proposed to link a benzoate moiety on the propargyl calixarene. The new reaction belongs to the so-called "Click Chemistry". This term groups gives many reactions that are characterised by same features such as: easy to be carry out, high yields and no byproducts.

The selected reaction was the Copper Catalysed Cycloaddition[9] between azides and alkynes, internal or terminal, that leads to the formation of 1,2,3-triazoles. If the reaction is carried out through the thermic route, there is the formation of both of the regioisomers (1,4 and 1,5) while in presence of Copper (I) salts, the formation of the 1,4 regiosiomer is exclusive. The mechanism of the reaction is catalysed by copper (I) that is introduced in the form of copper (II) sulfate and obtained in situ by reduction with sodium ascorbate.

The first step of this new synthetic pathway was the formation of the azide



4 **11**

Figure 30 – Synthesis of the derivative **11**.

on the methyl *p*-(bromomethyl)benzoate (**10**). The reaction was performed in acetone at 70°C, in presence of a large excess of sodium azide in order to efficiently displace the halogen atom.[10,11] The reaction was quantitative and at the end product **10** was used in the next step without further purifications.

The Copper Catalysed Azide-Alkyne Cycloaddition was carried out firstly on the monomer **4** and then on the calixarene platform, as already done with the Sonogashira reaction. The reaction was performed in DMF, in presence of $CuSO_4$, sodium ascorbate, excess of the azide **10**. The reaction was also activated with the help of the microwaves. After one hour, the TLC analysis showed the complete disappearance of **4**, so the reaction was worked up and product **11** was purified by flash chromatography on silica gel.

The ^{1}H NMR in *Figure 31* confirmed the successful outcome of the cycloaddition reaction. In particular the singlet at 7.56 ppm (pointed by

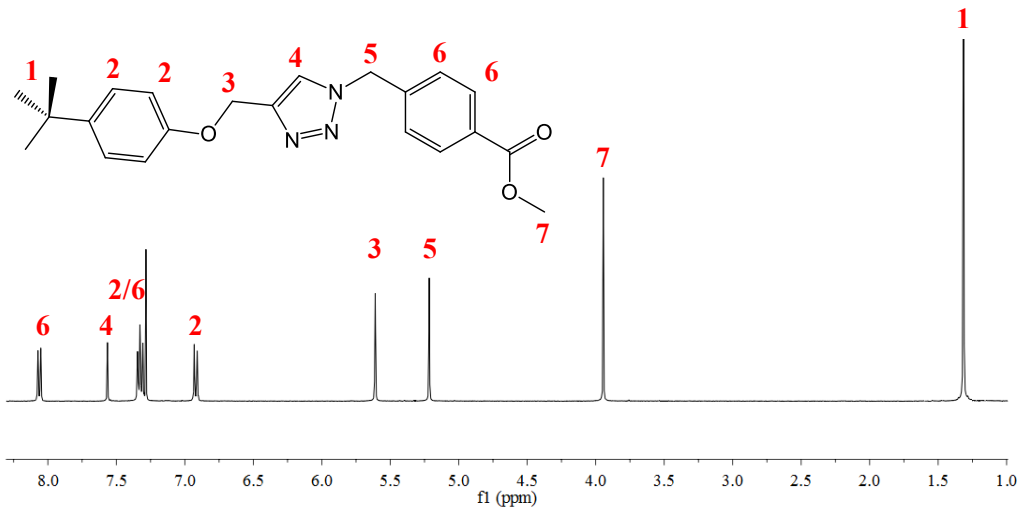
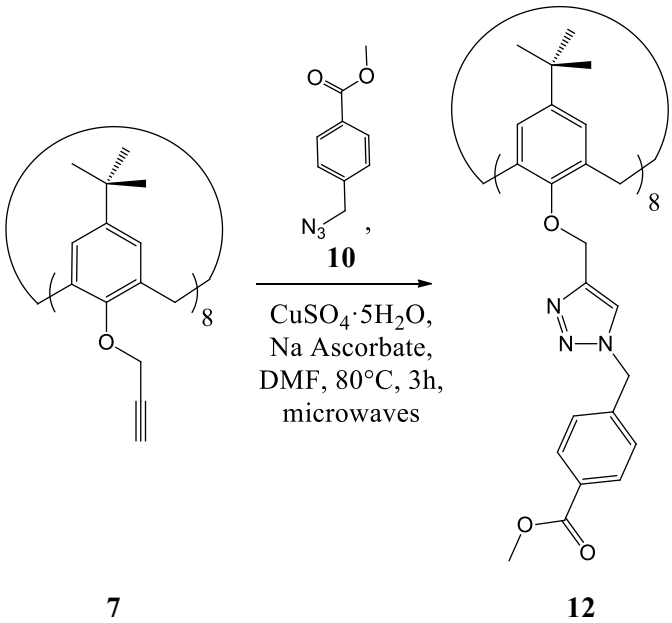


Figure 31 – ^{1}H NMR spectrum of compound **11** (400 MHz, $CDCl_3$, 25°C).

number 4) belongs to the hydrogen in position 5 of the triazole thus confirming the formation of the new aromatic heterocycle. Furthermore, the singlet at 3.94 ppm of the methyl ester and the two singlets at 5.61 ppm and 5.21 ppm of the two CH_2 groups linked to the new triazole



7 **12**

Figure 32 – Synthesis of the derivative **12**.

can be observed. The yield of the reaction was higher than 70%, and this encouraged the use of the same synthesis to the *p-tert*-butylcalix[8]arene (*Figure 32*).

The synthesis was therefore carried out starting from compound **7** and following the same conditions of the monomer. The reaction time was increased in order to favor the complete functionalisation of all the positions. At the end the product was purified by precipitation through a 1:1 mixture of dichloromethane/methanol and characterised by nuclear magnetic resonance spectroscopy.

Figure 33 shows the ^{1}H NMR spectrum of **12**. The spectrum is very similar to that reported in *Figure 31* of derivative **11** and in the same way it is possible to recognised the singlet of the hydrogen of the new triazole at 7.78 ppm. What is surprising is the singlet of the bridge that gives rise

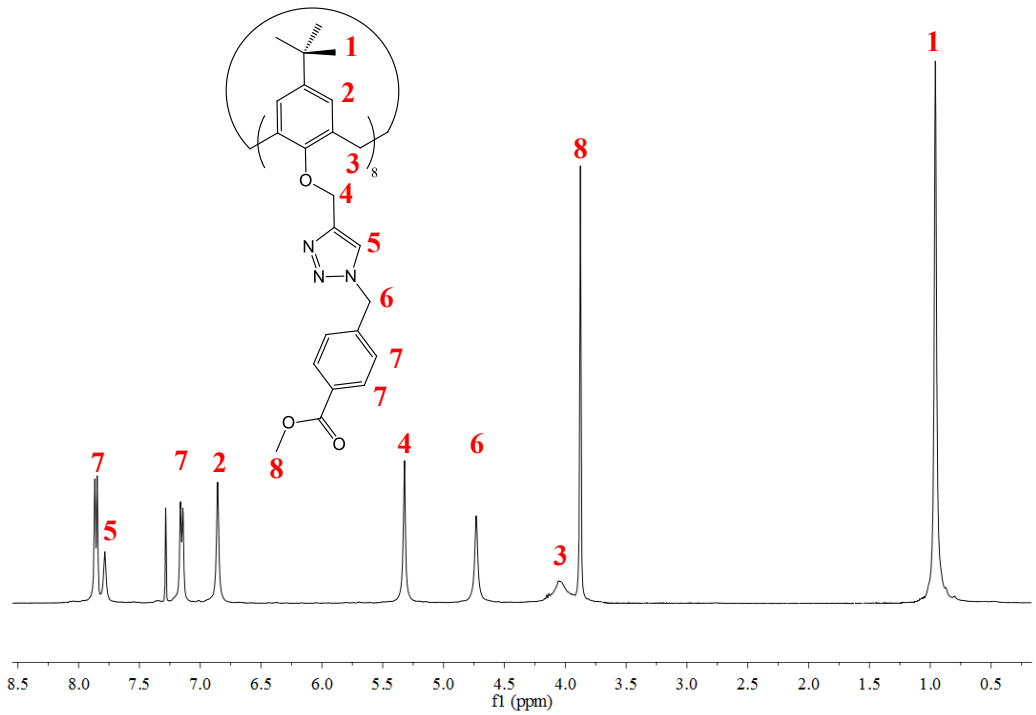


Figure 33 – ^{1}H NMR spectrum of compound **12** (400 MHz, $CDCl_3$, 25°C).

to a very broad signal at 4.00 ppm near the narrow singlet of the methyl of the ester function. This peculiarity gives some indications about the mobility of **12**. Apparently the high steric hindrance of the groups present at the lower rim (and t-Bu groups at the upper rim) causes a slowdown of the movement of the structure producing an enlargement of the signals near to the core of the molecule. On the other hand, the peaks belonging to further hydrogens from the core, for example the protons of the benzoate, are less influenced by this effect and so they generate narrow signals.

3.5.1 Star Polymer from compound 12

Compound **12** was used by the research group of Prof. Ciardelli and Pucci at the university of Pisa for the synthesis of the Star Polymer with the same conditions described in paragraph *3.3*.

After the synthesis of the linear arms of styrene/butadiene in cyclohexane, compound **12** was dissolved in a solution of THF and was added dropwise to the reaction mixture through a dropping funnel. Contrary to expectations after its addition, the solution changed colour and became turbid. At the end of the reaction the GPC analysis suggested the formation of no star polymer architecture.

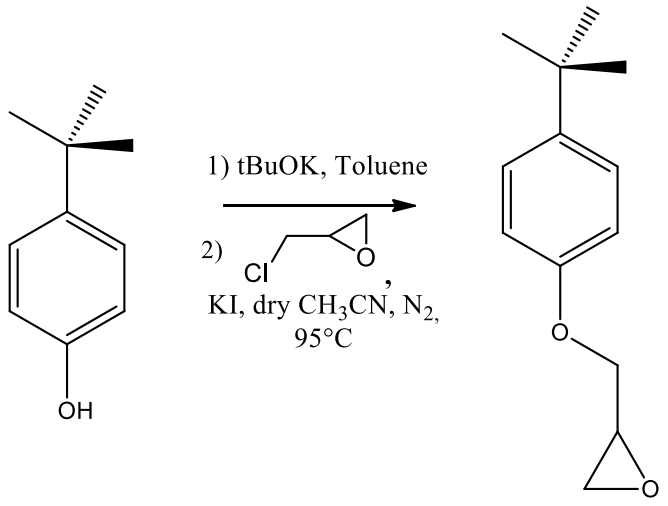
This unexpected result seems to be due to the insolubility of compound **12** in cyclohexane which prevent its reaction with the linear arms.

The research group in Pisa tried to modify the reaction conditions of the polymerisation to favor the solubility of compound **12**, but unfortunately no significant amounts of star polymers could be obtained.

3.6 Study of the epoxy function for the Living Anionic Polymerisation

In parallel with the studies described in the previous paragraphs, it was also investigated another reactive group, the epoxy function, that can be introduced onto the calix[8]arene platform for the binding with the living anionic polymer. A calix[8]arene derivative functionalised with eight epoxy groups could, in fact, allow the insertion of eight arms, so leaving therefore enough space for a complete functionalisation of all the calixarene subunits.

Epichlorohydrin was suggested as the best reagent to functionalise the *p-tert*-butylcalix[8]arene and again, to check the reactivity of the system, the first attempt was carried out on the simple monomer *p-tert*-butylphenol (*Figure 34*). The *p-tert*-butylphenol was dissolved in toluene in presence of a strong base like potassium *tert*-butoxide to favor



13

Figure 34 – Synthesis of the derivative **13**.

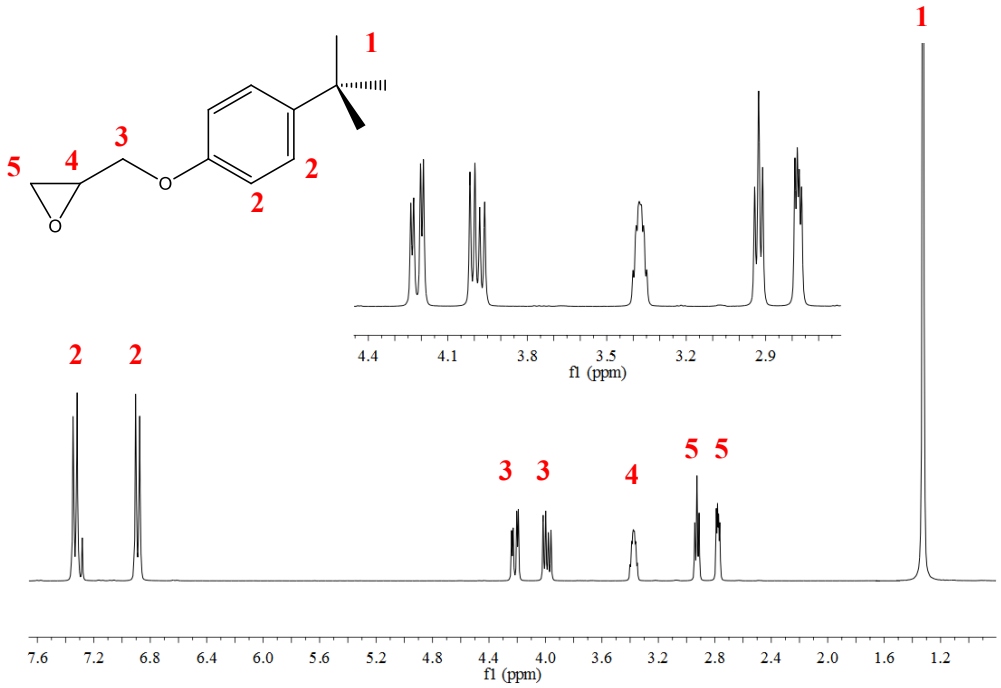


Figure 35 – ^{1}H NMR spectrum of compound **13** (400 MHz, $CDCl_3$, 25°C).

its complete deprotonation. Then the solvents was removed and epichlorohydrin, acetonitrile and potassium iodide in catalytic amount were added. The reaction was heated at 95°C under stirring until the TLC analysis showed the complete disappearance of the *p-tert*-butylphenol (about 18 hours).

The reaction was quenched by adding an acid aqueous solution, the organic phase separated and the solvent was removed under reduced pressure to give a yellow oil.

In *Figure 35* the ^{1}H NMR spectrum of the new derivative is reported. Due to the chiral center in position 4, the geminal protons in position 3 and 5 are not chemically equivalent. So the two doublet of doublets, respectively at 4.20 ppm and 4.00 ppm, belongs to the protons of the CH_2 group directly linked to the oxygen (number 3). Instead at higher fields

are present the signals of the protons of the CH_2 group of the epoxy group. At 3.35 ppm the protons in position 4 gives rise to a multiplet.

The yield of the reaction was very high (> 80%) so it was immediately repeated using *p-tert*-butylcalix[8]arene as starting material, under the same conditions. The number of equivalents of the reagents and the time of reaction were increased to functionalise completely the macrocycle.

At the end of the reaction a brown solid was isolated by simple precipitation, through a mixture of dichloromethane and diethyl ether, but the ^{1}H NMR spectrum of this derivative was characterised by very broad signals (*Figure 36*).

In the spectrum it is possible to recognise three different regions of the signals of the calixarene derivative: at high fields there is the peak of the *tert*-butyl group, at low fields the signal of the protons of the aromatic

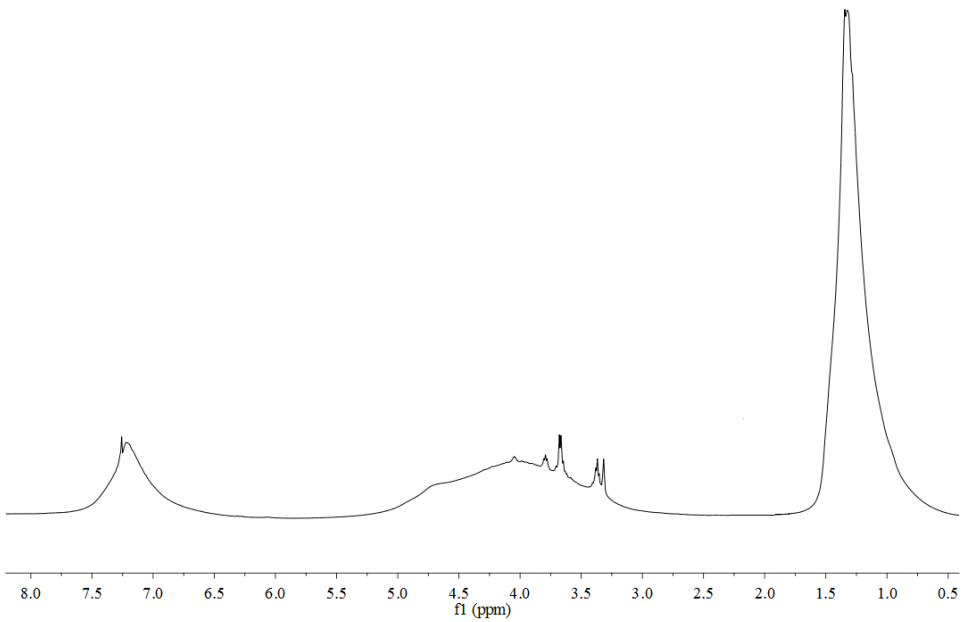


Figure 36 – ^{1}H NMR spectrum of the derivative from the reaction between epychlorohydryn and *p-tert*-butylcalix[8]arene (400 MHz, $CDCl_3$, 25°C).

nucleus and at the center of the spectrum the peaks of the chain similarly to *Figure 35*. However a so extensive broadening was rather surprising and unexpected. Usually, in calixarene chemistry, such broad spectra are indicative of a reduced conformational mobility or of the presence of polymeric species when polyvalent calixarenes react with di/polyfunctional reagents (such as in the case of epichlorohydrin) and suggested that in the reaction there were some side reactions that prevent the formation of the desired product. The ESI-MS analysis could not help to shed a light on the nature of the precipitate, also because it was very insoluble in the solvents generally used for this technique.

Excluding the possibility to have reduced conformational mobility since the groups introduced at the lower rim are not characterised by a relevant steric hindrance, we reasoned that the broad spectra are more probably due to possible cleavage of the epoxy groups like in *Figure 37*. The epoxy groups might be cleaved by the attack of a nearby phenoxide present on another molecule of calix[8]arene (intermolecular attack) or on the same macrocyclic structure (intramolecular attack) in a sort of

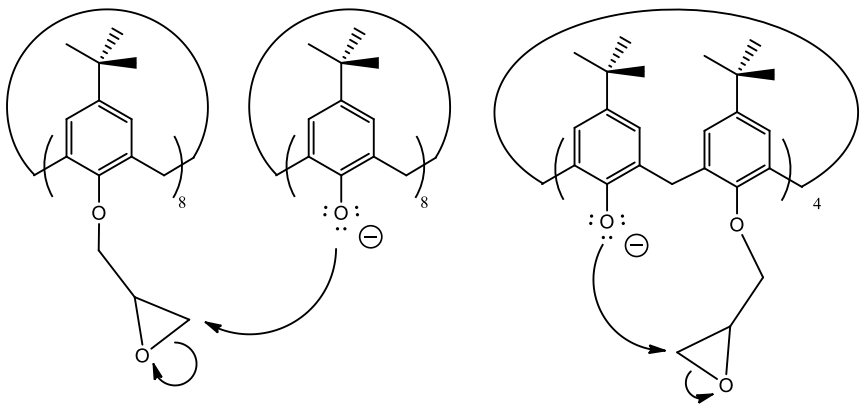
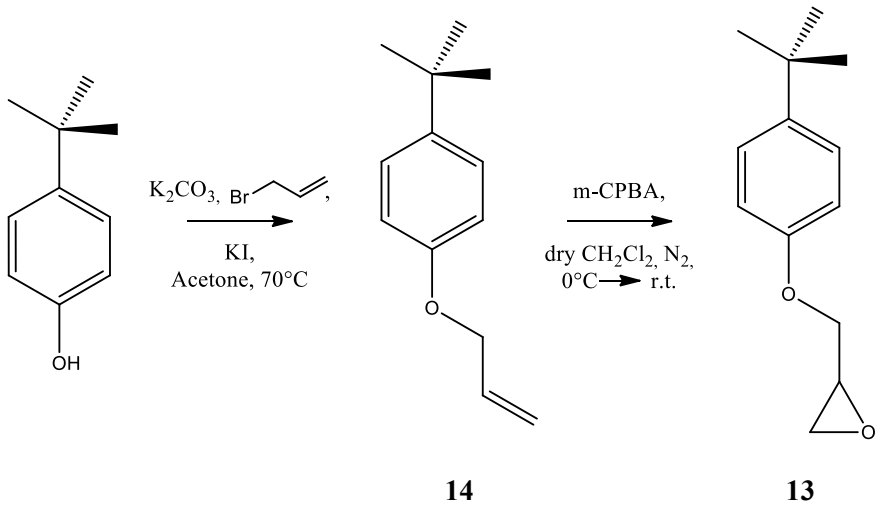


Figure 37 – Inter- (left) and intra- (right) molecular reactions responsible of the opening of the epoxy groups in the *p-tert*-butylcalix[8]arene.

copolymerisations. It is, in fact, well-known that epychlorohydrin is used in anionic polymerisation.[12] Although it could not be ascertained without doubts the nature of the product, it was established that the desired product was not formed in the reaction. However, it appears more reliable, on the basis of absence of peaks in the ESI-MS spectrum, that a copolymer was formed.

To arrive to the target product, it was therefore necessary to follow a different synthetic path. The reaction of functionalisation with allyl bromide of the *p-tert*-butylcalix[8]arene is well documented in literature,[13] so it was planned to oxidise the perallylated calix[8]arene to obtain the final product. Once again, the reaction was firstly investigated on the monomeric model also because the oxidation of a terminal double bond is more difficult compared to a more substituted one.

In *Figure 38* the route to reach product **13** is illustrated. The allylic group was introduced onto the phenol through a procedure present in the literature.[14,15] The phenol was reacted with allyl bromide in presence of a

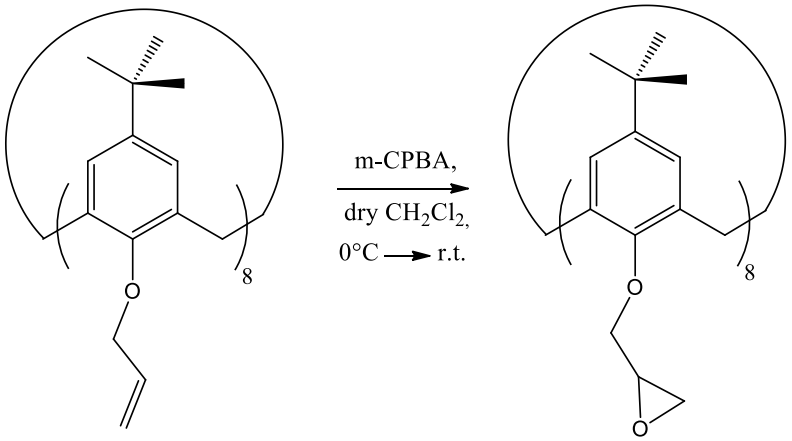


14 **13**

Figure 38 – New synthetic pathway to obtain product **13**.

base, potassium carbonate, in acetone at 70°C. In about 15 hours the reaction was completed and the formation of product **14** was confirmed by the ^{1}H NMR spectrum. In the literature it is reported the reaction of epoxidation of a phenol derivative very similar to product **14** by using the 3-chloroperbenzoic acid (m-CPBA).[16] Since the reaction conditions are rather soft, it was selected this reagent to study this oxidation step.

The reaction was carried out in dry dichloromethane at room temperature in inert atmosphere. After about 24 hours the reaction was quenched, the product was purified by flash chromatography on silica gel. Its presence was confirmed for comparison with the spectrum of the derivative **13** previously synthesised. The low yield of this reaction (about 40%), are related with the low conversion as the initial reagent was recovered in about 30% of the initial quantity. However, the oxidation reaction on the *p-tert*-butylcalix[8]arene completely functionalised with allyl groups was performed, considering that the calix[8]arene can be purified by simple precipitation avoiding the separation by chromatography that could be the



15 **16**

Figure 39 – Synthesis of derivative **16**.

origin of the loss of part of the product.

The reaction of oxidation was carried out at room temperature for a period of 24 hours. At the end the solution was washed with brine to remove the 3-chloroperbenzoic acid in excess, the solvent was removed under reduced pressure and the product was purified by precipitation through a mixture of dichloromethane/diethyl ether. The isolated precipitate was analysed by proton nuclear magnetic resonance, and the spectrum is reported in *Figure 40*.

The spectrum of this compound is also characterised by broad peaks but, in contrast with that one of *Figure 36*, it is now possible to assign all the signals. The residual broadness of these signals might be attributed to the presence of several (8) chiral centers.

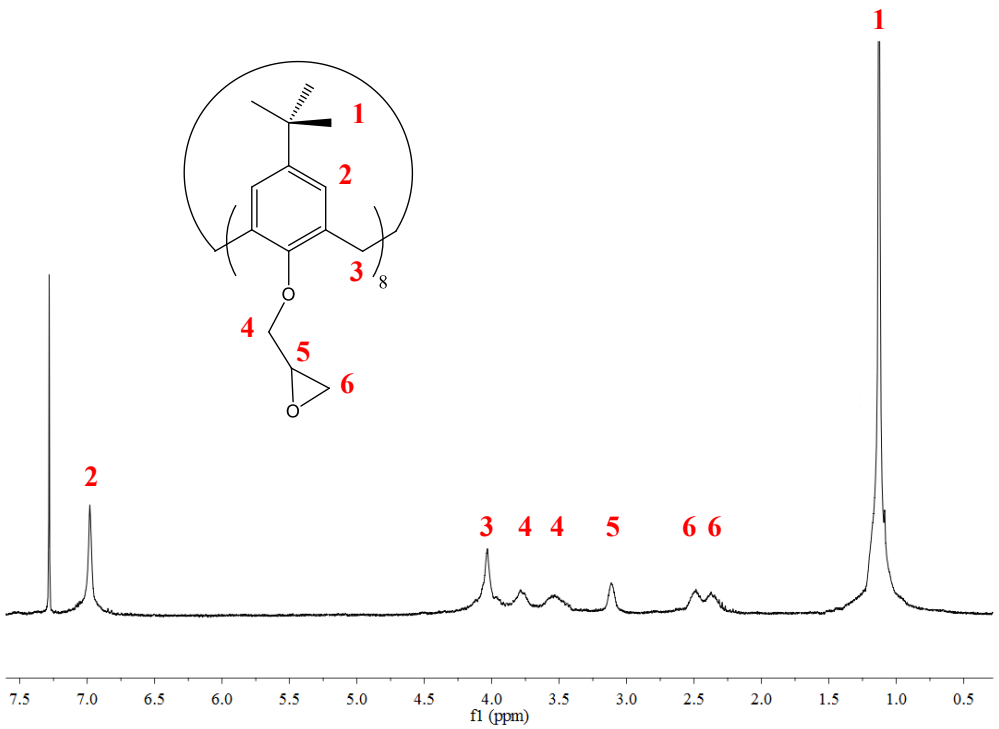


Figure 40 – ^{1}H NMR spectrum of compound **16** (400 MHz, $CDCl_3$, 25°C).

In details, at 4.03 ppm it is possible to observe the singlet of the methylene bridge, while between 4.00 ppm and 2.00 ppm are present the peaks of the oxyrane ring. The attribution of the signals were done having the spectrum of the monomer **13**, previously synthesised, as a reference. The spectrum of **16** also shows no presence of residual signals due to vinylic protons between 6 ppm and 5 ppm, proving that all the double bonds had disappeared. However, even though compound **13** gives rise to a clean ESI-MS spectrum in spite of the high reactivity of the oxyrane ring, for compound **16** it was impossible to evidence the molecular peak having no direct proves of the presence of all the eight epoxy groups at the lower rim of the macrocycle.

This synthetic route through the oxidation of the allyl groups of the calix[8]arene leads, however, to a maximum yield of 20% and the purification of the product from the crude is not so easy.

3.6.1 Study of the reactivity of the epoxy function

In parallel to the preparation of compounds **13** and **16** it was also studied the reactivity of the epoxy function under the coupling conditions used for the synthesis of the star polymers.

The reaction of coupling was carried out using *n*-butyllithium for the reasons explained previously in the section *3.3*. As substrate of the reaction, monomer **13** was used since on this monomeric model it was easier to understand, compared to the calixarene, whether the reaction takes place and in which yield.

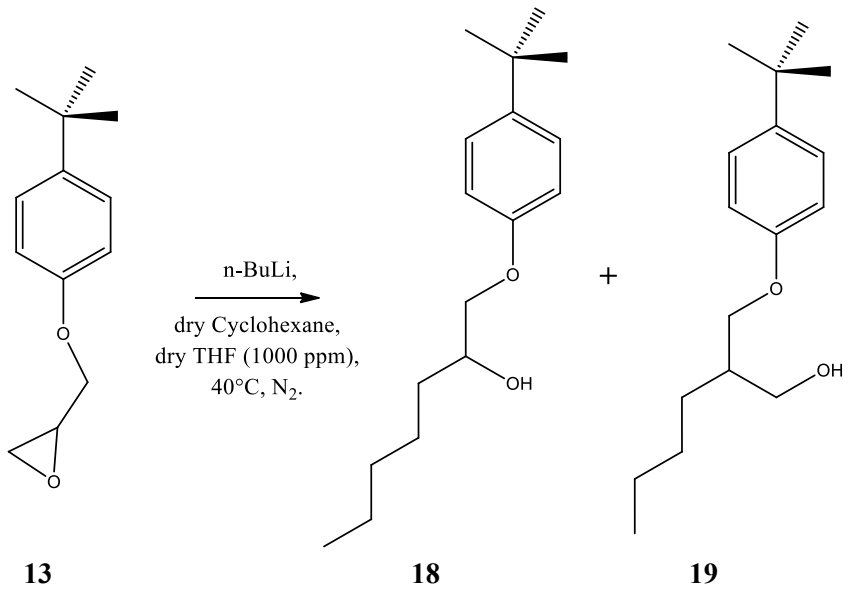


Figure 41 – Reaction of functionalisation with n-BuLi.

The conditions of the reaction are reported in *Figure 41*. The coupling was run in a mixture of cyclohexane and THF (1000 ppm) at the temperature of 40°C. *n*-BuLi was added in stoichiometric amount to replicate the conditions of the synthesis of the star polymer. It is usually quite accepted that the nucleophile attack onto a terminal oxyrane ring is strongly favored on the less substitute (primary) carbon even though an attack on the other side is not excluded. So the reaction should lead to the formation of a large amount of product **18** and a much lower quantity of **19**.

A first analysis of the crude of the reaction by ^{1}H NMR showed a significant presence of signals of the epoxy group, indicating that the starting reagent was not completely consumed. Moreover in the region between 6.5 and 5 ppm were also present signals not associated to the final products. In this area in general fall the signals of double bonds, thus suggesting that during the quenching of the reaction at ambient

temperature an elimination of water had taken place. To figure out the nature of the new species formed in the reaction, it was recorded an ESI-MS spectrum (*Figure 42*).

The spectrum was recorded on positive ions and showed the main peaks at 287.5, 379.6 and 493.7 amu The first peak corresponds to the adduct with sodium of products **18** and/or **19**, the other two instead are separated respectively by a value of 92 and 228 amu from the first peak.

According to these data, it can be inferred that the deprotonated oxygen of **18** gives a nucleophilic attack on the CH_2 group linked to the phenolic oxygen, displacing the phenoxide anion and resulting into an epoxy derivative with a long chain and a molecular weight of 114 amu. The reaction is favored by the good leaving group capacity of the phenoxide anion. The presence of such a novel electrophilic oxyrane molecule, quite

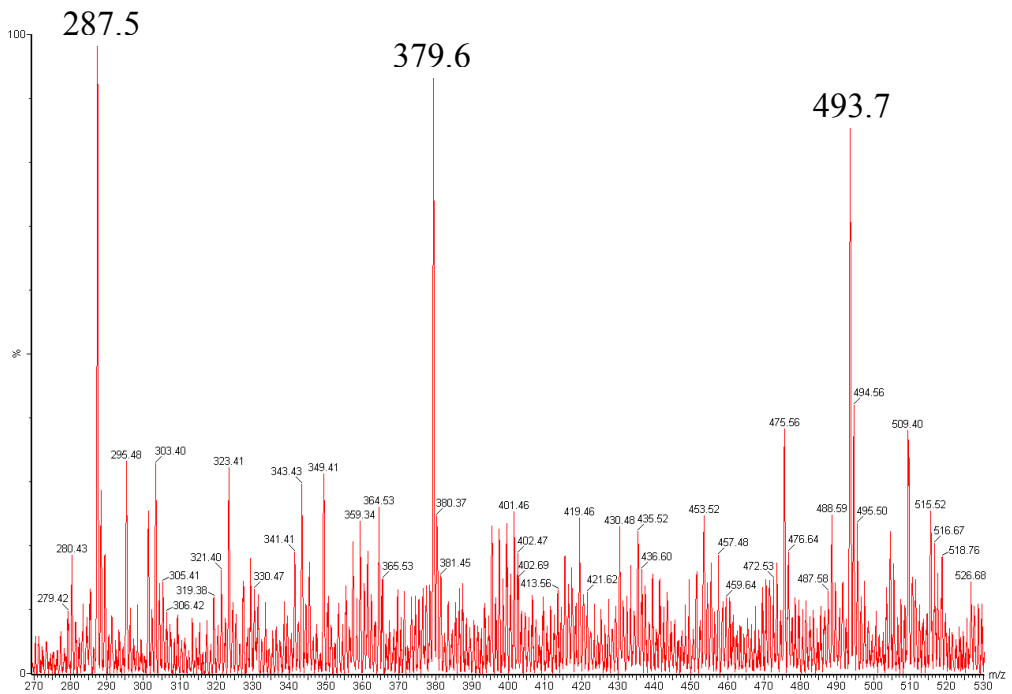


Figure 42 – ESI-MS spectrum of the crude product.

reactive, in solution apparently may give rise to a series of by-products by reaction with the alkoxide of **18**. By addition of the alkoxide **A** to the epoxy derivative, a molecule (**B**) with a molecular weight of 378 forms, as testified by the peak at 379 m/z in the ESI(+) spectrum corresponding to the $[M+H]^+$ ion of the derivative **B**. Hence, it could conceivably be hypothesised that peak 493.7 has a similar origin, being the result of the reaction of another epoxide derivative with **B**. This is proved by the formation of the species **C** of molecular weight 492.

Since the elimination mechanism shown in *Figure 43*, is favored by the phenol group in α position with respect to the oxyrane function we speculated that these side reactions may be avoided in a situation where

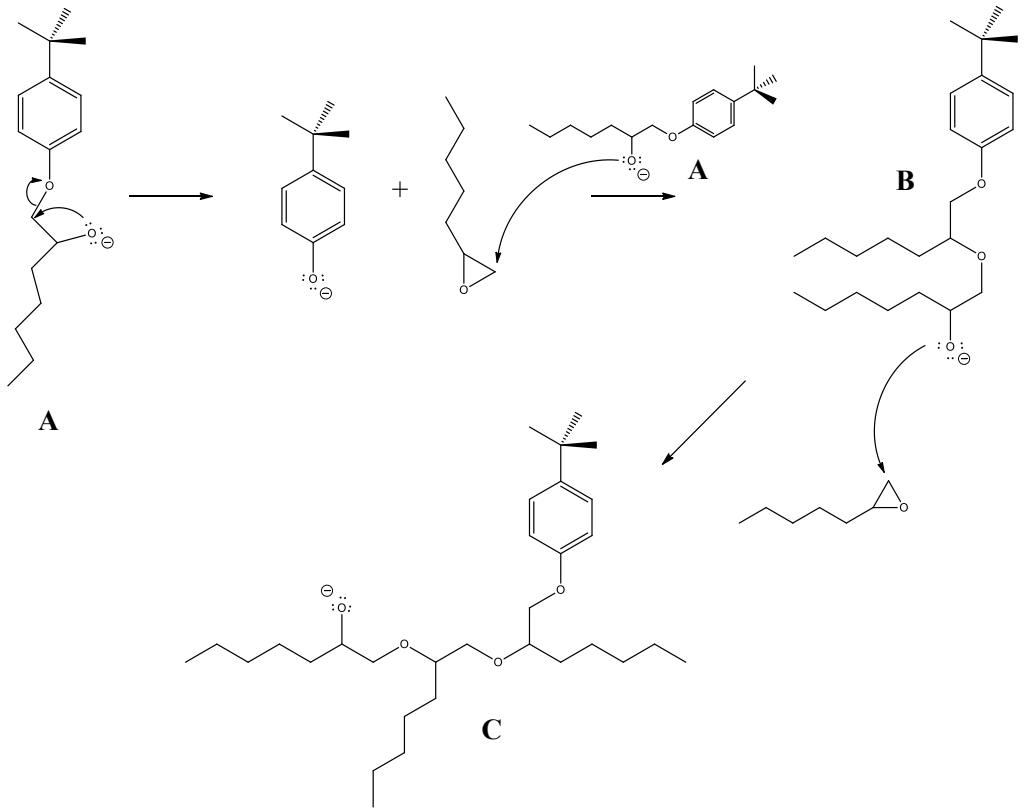


Figure 43 – Side reaction of product **18**.

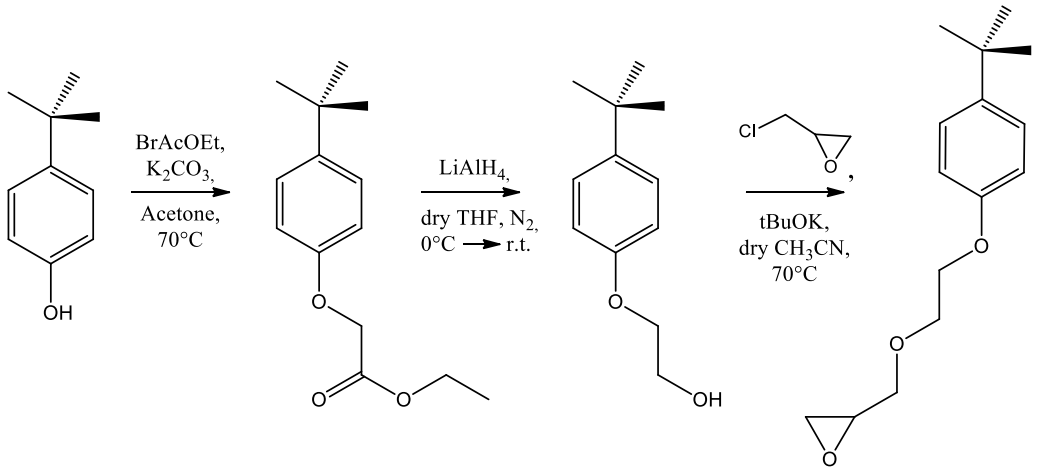


Figure 44 – Synthesis reaction of product **22**.

the epoxy group is moved apart from the phenol. For these reason product **22** was synthesised following the synthetic route in *Figure 44*.

The *p-tert*-butylphenol was functionalised with ethyl bromoacetate, and then the ester group was reduced with lithium aluminum hydride to alcohol **21**. In the end this derivative was functionalised with epychlorohydrin under the same conditions reported in paragraph *3.6* for the monomer **13**.

The new product **22** was subsequently tested in the reaction with *n*-BuLi. It was dissolved in dry cyclohexane and dry THF in a ratio of 100:1 at 40°C and then the organo-lithium compound was added dropwise to the solution. The amount of THF was raised compared to cyclohexane in order to increase the reactivity of the *n*-BuLi. This increase led to the desired effect and the TLC analysis showed that derivative **22** was completely consumed.

The crude reaction mixture was analysed by ESI-MS. The spectrum in *Figure 45* shows two main peaks: the first one at a value of 331.42 m/z

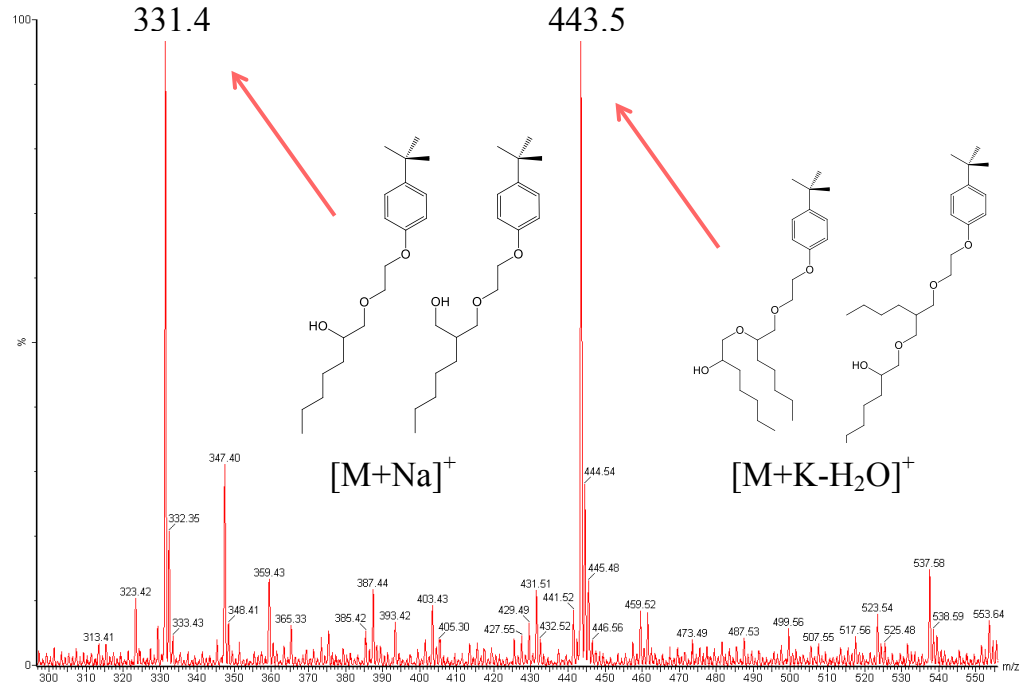


Figure 45 – ESI-MS spectrum of derivative **22** after the reaction with *n*-BuLi.

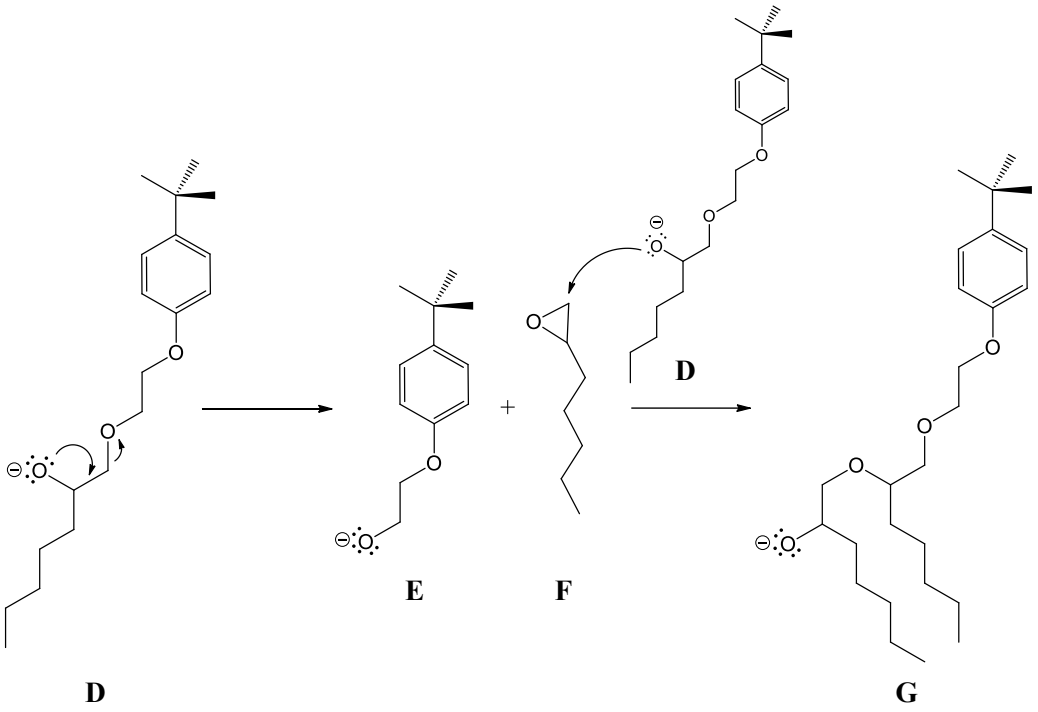


Figure 46 – Mechanism of elimination on the new derivative.

belongs to the desired product, while the other very important peak has a value of 443.5 amu. This second peak was attributed to the products of the side reactions that take place always through an elimination process.

In *Figure 46* the mechanism of formation of this high molecular mass product is highlighted. Also in this case the deprotonated oxygen in **D,** derived from the opening of the oxyrane ring by attack of butyl lithium, attacks the α carbon displacing a phenoxyethanol anion (**E**) and generating a novel epoxy derivative (eptene oxide, **F**). The simultaneous presence in solution of this novel epoxide (**F**) and of the deprotonated product **D** gives rise to a novel addition product **G**, which gives the observed peak in the mass at 443.5 m/z ($[M+H]^+$).

The separation of the epoxy group from the benzene ring has therefore not limited the elimination reactions and the side products of this coupling reaction that should have been straightforward. Furthermore the ^{1}H NMR spectrum recorded on the crude product shows peaks between 6 and 5 ppm like already observed for the monomer **13**, so probably the epoxy group in presence of the *n*-BuLi also undergoes some other not well identified elimination reactions.

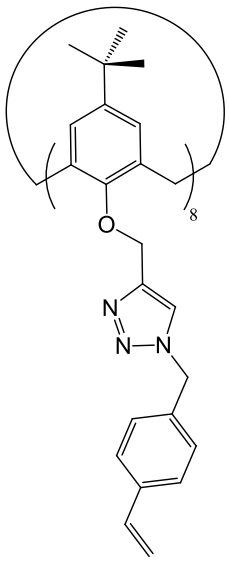
The findings of this study provide a deeper understanding of the reactivity of epoxy groups towards carboanionic alkyl chains such as butyl lithium. However due to the side reactions described and also due to the difficulties to obtain the calixarene derivative **16** (functionalised with epoxy groups), it was decide not to continue on this line and that epoxides are not good candidates for the synthesis of star polymers.

3.7 Calixarene core systems for Radical Polymerisation

The methods of controlled radical polymerisation are ideal for the synthesis of polymers as additives in lubricants because they lead to materials with controlled molecular weight and with rather narrow distribution of molecular weights.

These features, in fact, give to the VII lower shear stress index and therefore better mechanical stability, compared to analog products synthesised with the conventional radical polymerisation. Moreover, these technique can be used to synthesise complex structures such as star polymers,[17,18] that are characterised by very high thickening power.

In the following of this chapter, we will describe our efforts to design and synthesise calixarene derivatives potentially able to react with linear polymers grown with radical polymerisation, thus exploiting an "Arm-First" approach to create Star Polymers. For their possible use as oil additives, the new macrocycles should be able to react with radicals, so double bonds activated to radical polymerisation should be present such as those of styrenes or acrylates etc. Moreover, they should also be soluble in mineral oil. In fact, the polymerisation should ideally takes place directly in the mineral oil as already described in few existing patents.[19] This will also allow to make the process more sustainable preventing the use of large amount of solvents and thus facilitating a possible industrial scale-up.



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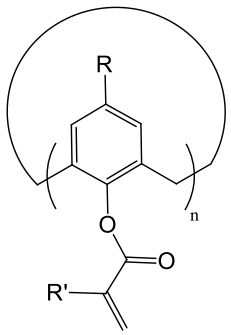


25: R = -tBu. R' = -H, n = 8.

26: R = -tBu. R' = -CH_3, n = 8.

27: R = -C_8H_{17}. R' = -CH_3, n = 8.

28: R = -$C_{12}H_{25}$. R' = -CH_3, n = 4,5,6,7,8.

Figure 47 – Calixarene derivatives for radical polymerisation.

The different calixarenes synthesised for this work are illustrated in *Figure 47*. The first moiety introduced with success onto the calix[8]arene platform are styrene groups such as in the derivative **24**. This vinyl moiety present is known to be very reactive in the radical polymerisation. The synthesis of this derivative followed the route previously described for **12**. On the other hand, for the synthesis of calixarenes **25**-**28** on the right of *Figure 47*, the corresponding *p*-alkylcalixarenes were functionalised at the lower rim through an esterification reaction with acryloyl chloride or methacryloyl chloride. In this series of compounds, the length at the upper rim of the chain was gradually increased to favor the solubility in mineral oil. Particularly interesting is the mixture of compounds **28**, synthesised by a mixture of calixarenes with very long and branched chains at the upper rim. The methods and the procedures to synthesise this kind of calixarenes will be discussed in *Chapter 4*.

3.7.1 Calixarene derivatives for Radical Polymerisation

The first compound to be synthesised was **24**. In the last years, it was studied the functionalisation of the *p-tert*-butylcalix[8]arene with 4-vinylbenzyl chloride. Unfortunately, under basic conditions, 4-vinylbenzyl chloride is too reactive and gives rise to secondary reactions of decomposition, thus avoiding the formation of the product.

However, in analogy with what previously (see paragraph *3.5*) and successfully done with methyl *p*-(bromomethyl)benzoate, it was planned to introduce the styrene moiety by exploiting the Copper Catalysed Azide-Alkyne Cycloaddition.

First of all, the 4-vinylbenzyl chloride was converted into the corresponding azide **23** following a procedure present in literature.[20] The 4-vinylbenzyl chloride was dissolved in a mixture of acetone : water = 9 : 1, the solution was cooled to 0°C and sodium azide

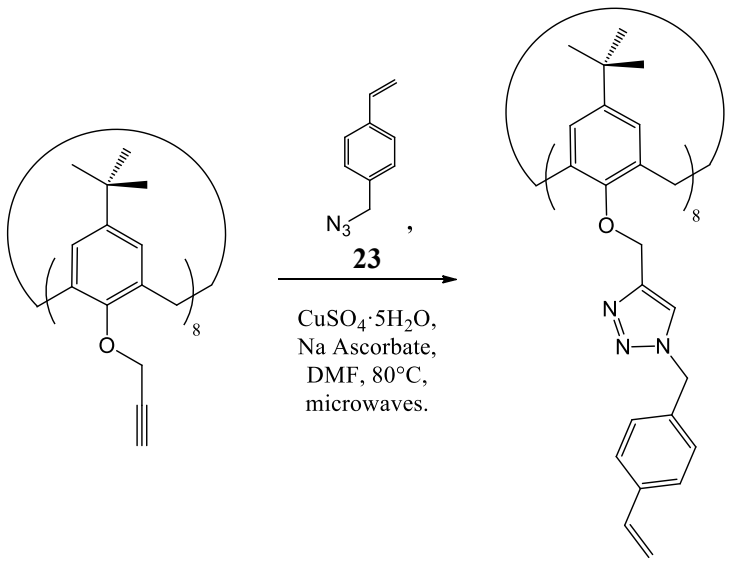


Figure 48 – Synthesis of derivative **24**.

was added in large excess. The reaction was stirred for 15 hours and after work up derivative **23** was used in the following step without further purifications.

The *p-tert*-butylcalix[8]arene functionalised with propargyl groups (**7**) was subjected to the Copper Catalyzed Azide-Alkyne Cycloaddition with azide **23** using similar operative conditions to those previously described in this chapter (see paragraph *3.5*). The use of the microwave irradiation to activate the reaction allows to consistently reduce the reaction time and to increase the final yield of **24** also by reducing the amount of decomposition products. At the end, the reaction was cooled to room temperature and filtered to remove the inorganic salts. The solvent was then removed under reduced pressure and the crude product was purified by precipitation with a mixture of dichloromethane/methanol.

The ^{1}H NMR spectrum recorded on the precipitate confirmed the

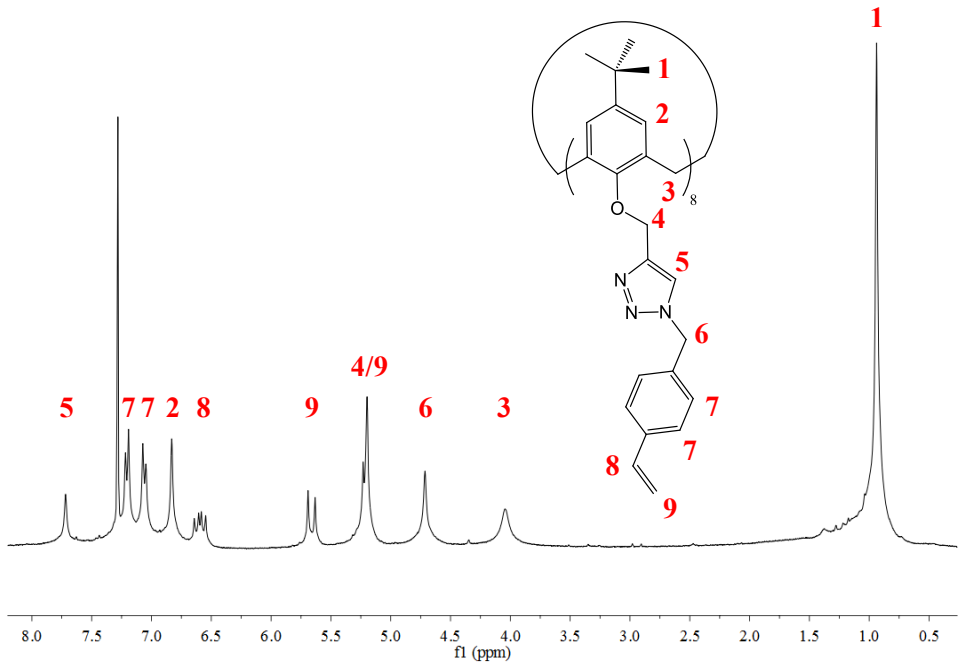
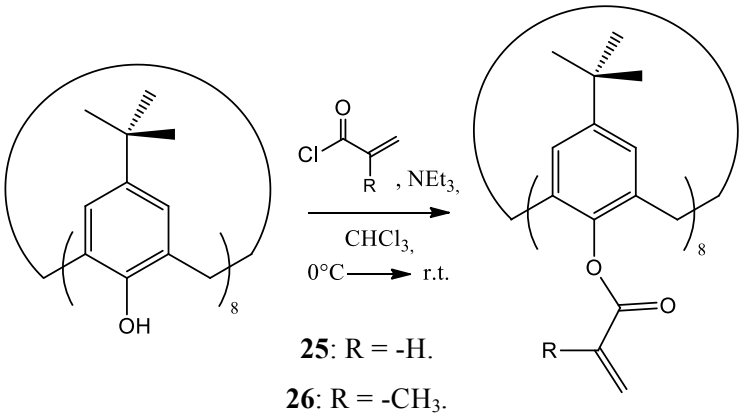


Figure 49 – ^{1}H NMR spectrum of compound **24** (300 MHz, $CDCl_3$, 25°C).

successful formation of the product **24** (*Figure 49*). The signals of the propargyl group disappeared while it is possible to observe the main peaks of the new function introduced at the lower rim. Starting from low fields, peak number 5 points out the singlet of the hydrogen of the new triazole unit, then there are the two doublets belonging to the aromatic protons of the vinylbenzyl ring and, shifted a little to higher fields (between 6.7 ppm and 5 ppm) are present the signals of the vinyl group. At 6.60 ppm resonates a doublet of doublets belonging to the hydrogen in position 8 which couples with the two terminal hydrogens of the alkene. Instead the hydrogen in position 9 (trans to 8) resonates at 5.66 ppm giving a clean doublet because it couples with hydrogen in 8 with a high J constant while the germinal coupling constant is close to zero. The vinylic proton in cis with 8 instead resonates under the singlet of the CH_2 group in position 4, as supported by the HSQC spectrum. The product was isolated in a yield of about 60%.

Having discussed how product **24** was obtained, the next section of this paragraph addresses the synthesis of product **25** and **26** (*Figure 50*).



25: R = -H.

26: R = -CH_3.

Figure 50 – Synthesis of derivatives **25** and **26**.

The reaction of esterification at the lower rim of the *p-tert*-butylcalix[8]arene was performed following an already existing procedure in literature.[21] The calix[8]arene was dissolved in chloroform, later it was added trietylamine in large excess to favor the deprotonation of the hydroxyl groups and to neutralise the HCl that is developed by the reaction. The mixture was cooled to 0°C before adding the acyl chloride because the reaction is greatly hexothermic. The reaction mixture was stirred for 24 hours and it was then quenched with a solution of sodium bicarbonate.

Both product **25** and product **26** were purified by simple precipitation through a mixture of dichloromethane/diethyl ether = 1:1 and their identity and purity were confirmed by ^{1}H NMR. In *Figure 51* the ^{1}H NMR spectrum of product **25** is reported, while in *Figure 52* that one of **26**.

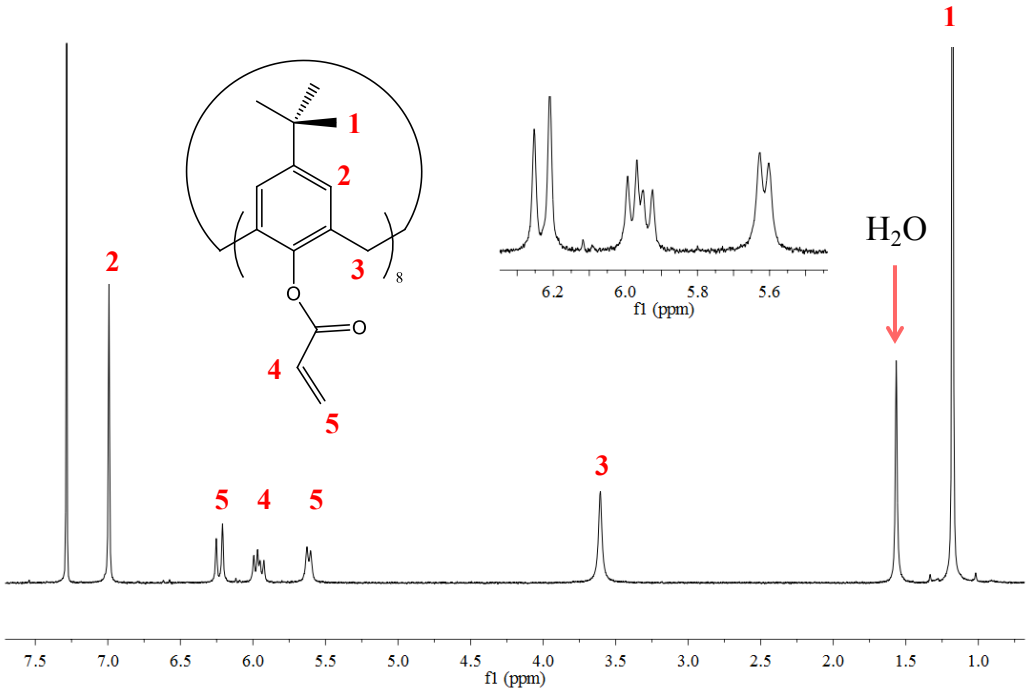


Figure 51 – ^{1}H NMR spectrum of compound **25** (400 MHz, $CDCl_3$, 25°C).

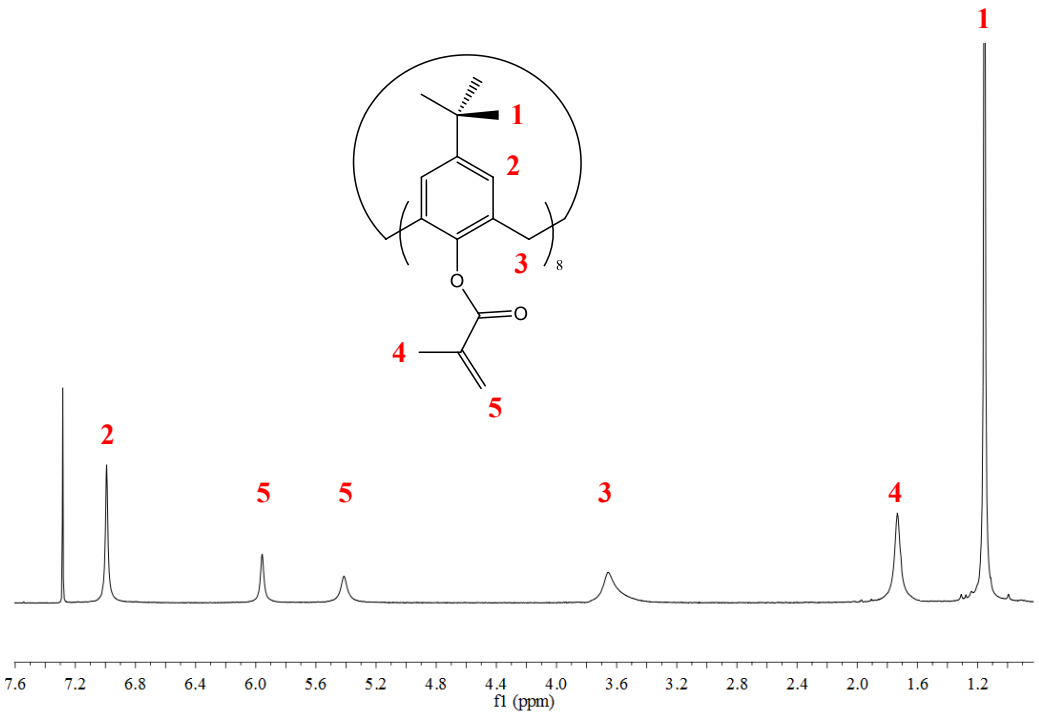


Figure 52 – ^{1}H NMR spectrum of compound **26** (400 MHz, $CDCl_3$, 25°C).

The first spectrum is characterised by narrow peaks. At 6.23 ppm and 5.61 ppm resonate the two doublets of the terminal hydrogen (5) of the alkene which are coupled with the hydrogen in position 4 but not to each other in a similar way to product **24**. The other peaks, belonging to the calixarene structure, are marked with numbers 1, 2 and 3.

The spectrum of compound **26**, instead, is characterised by broader signals compared to **25**. The main difference with respect to the previous derivative is represented by the terminal hydrogens of the alkene that give rise to two singlets at 5.96 ppm and 5.41 ppm, due to the absence of the hydrogen in position 4. The methyl group generates a singlet at high fields marked with number 4.

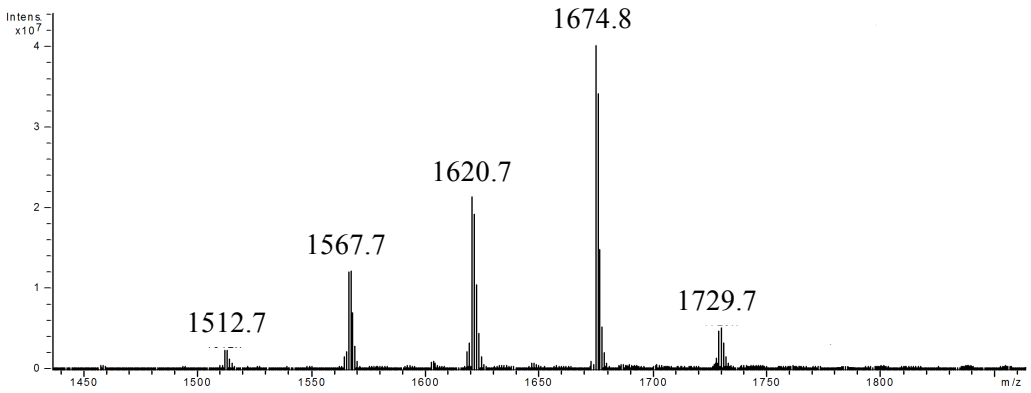


Figure 53 – APPI-MS spectrum of compound **25**.

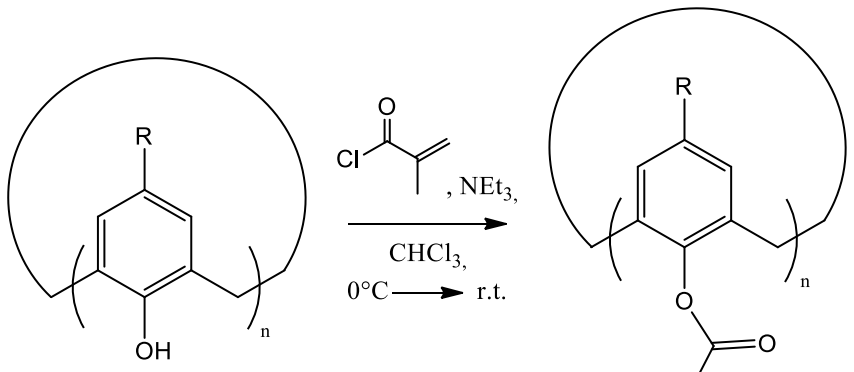
The MS spectra of compound **25** and **26** were recorded to ascertain the complete functionalisation of these derivatives, but they showed the presence of partially functionalised compounds. *Figure 53* shows the APPI-MS spectrum of compound **25**, the peak at the value of 1729.7 belongs to the $[M+H]^+$ adduct of the product completely functionalised. Instead the other peaks, with higher intensity, belongs to products partially functionalised and lacking of 1 to 4 acrylate groups. However, these data must be interpreted with caution because the ^1H NMR spectra of this compound did not show any suggestions of partial intermediates. Our hypothesis is that in the ionisation chamber, due to the very high temperature, a hydrolysis reaction with the elimination of the acrylate takes place. Similar observations were also collected for product **26**.

The products **24**, **25** and **26** were sent to the research group of Prof. Laus for studies on the coupling reaction with linear arms synthesised by radical polymerisation in mineral oil. Unfortunately, the calixarene cores demonstrated to be insoluble in the mineral oil, stopping any further studies on this compounds. This observation was obviously quite disappointing and unexpected, since generally the complete

functionalisation of the hydroxyl groups favors the solubility in apolar solvents and a similar trend was expected for the mineral oil. However, in order to try to fix this problem of solubility, it was decided to introduce such acrylate units at the lower rim of calixarenes bearing longer and branched chains at the upper rim.

3.7.2 Calixarene derivatives for radical polymerisation bearing long chains at the upper rim

Previous studies on acrylate derivatives of calixarene, reported in paragraph *3.7.1*, were conducted only on the simplest *p-tert*-butylcalix[8]arene. In this paragraph it will be also described the syntheses and characterisations of acrylate derivatives of *p-tert*-octylcalix[8]arene and of mixtures of *p*-dodecylcalix[n]arene (*Figure 54*). For these calixarene cores it was decided to carry on the reaction of esterification with methacryloyl chloride instead of acryloyl chloride, because the first lead to a slightly more lipophilic



27: R = -C_8H_{17}, n = 8.

28: R = -$C_{12}H_{25}$, n = 4,5,6,7,8.

Figure 54 – Synthesis of derivatives **27** and **28**.

functionalisation of the calixarene increasing the solubility in oil.

Besides, this type of reaction (esterification) has several advantages compared to the CuAAC reaction, being faster, cheaper and avoiding the use of potentially dangerous reagents such as azides (that can be explosive), issue particularly relevant especially in view of a possible industrial scale up.

Moreover, by using the methacryloyl chloride, instead of the acryloyl chloride, it is possible to introduce at the lower rim of the calixarene platform a slightly more lipophilic substituent and this might lead to an increase of the solubility in oil.

Compound **27** was synthesised starting from the *p-tert*-octylcalix[8]arene. The synthesis of this macrocycle was studied for the first time by John H. Munch in 1977,[22] however the general procedure was optimised in the last years in this research group to reach higher yields of the macrocycle with eight units.[23] The *p-tert*-octylphenol was mixed and heated with aqueous formaldehyde solution and sodium hydroxide at 120°C for one hour. In the second step xylenes was added and the reaction was heated at reflux for four hours in order to remove water from the reaction vessel and favor the cyclisation of the oligomers. TLC and MS analysis could evidence that, at the end of the reaction, the solution was a mixture of calix[8]-, calix[6]arene and a small quantity of calix[4]arene. However, thanks to the procedure reported in the literature it is possible to separate quite easily the octamer from the other macrocycles through a simple crystallisation.[24]

So, *p-tert*-octylcalix[8]arene was functionalised at the lower rim using the same conditions employed for compounds **25** and **26**. The product was

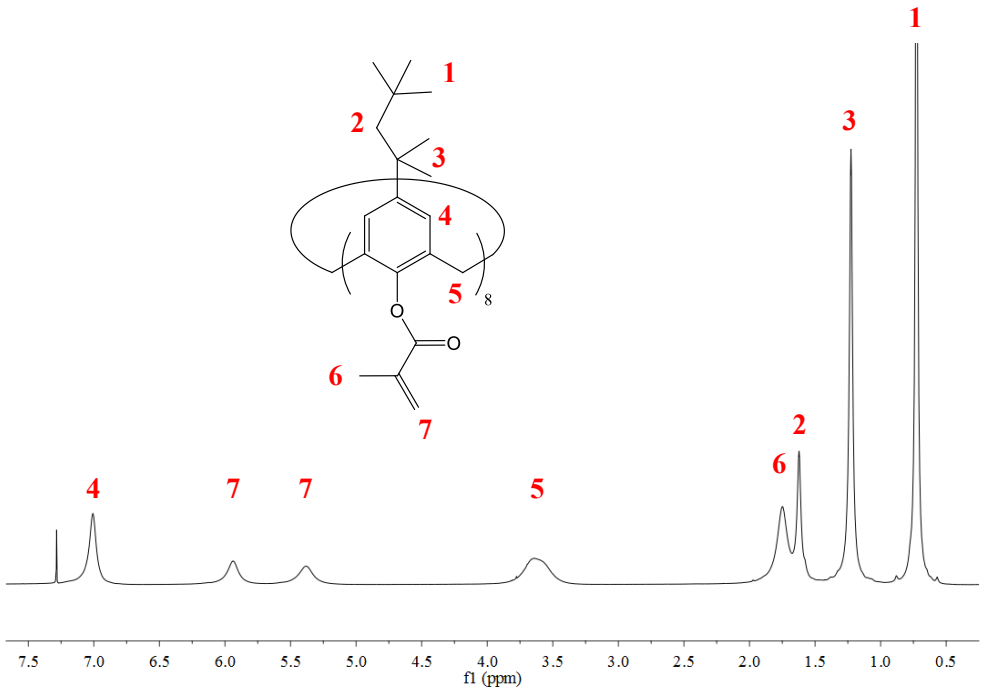


Figure 55 – ^{1}H NMR spectrum of compound **27** (400 MHz, $CDCl_3$, 25°C).

purified by precipitation and its ^{1}H NMR spectrum was recorded. *Figure 55* reveals that the desired exhaustive introduction of the methacryloyl group at the lower rim took place. The spectrum is very similar to that of compound **26**: the peaks of the aliphatic chain are located at high fields, while at 3.65 ppm is present the singlet of the methylene bridge characterised by fair broadening. As already observed for **26**, the two hydrogens in position 7 give rise to two singlets at 5.94 ppm and 5.37 ppm. At lower fields (7.00 ppm) it is possible to observe the typical singlet integrating for two protons of the aromatic hydrogen of the calixarene platform. Unfortunately it was not possible to obtain a mass spectrum of **27** to confirm the complete functionalisation of all the eight positions since this derivative was not soluble in the solvents (MeOH or ACN) generally used in ESI-MS. However the integration of

the peaks of the ^{1}H NMR spectrum in *Figure 55* was correct thus supporting that the macrocycle is completely functionalised.

Moving on now to consider derivative **28**, it was synthesised using a mixture of *p*-dodecylcalix[n]arenes. This special composition was obtained from the condensation between *p*-dodecylphenol and formaldehyde and it will be discussed in more details in the next chapter. Thanks to the long and branched chain in para position of the dodecylphenol, the final product results highly soluble even in very apolar solvents. However, the great variability of the substituents at the upper rim of these calixarenes makes no possible the separation of the macrocycles of different size by simple crystallisation or precipitation. So, in contrast with the other derivatives synthesised previously, product **28** is formed by a mixture of calix[n]arenes with n variable between 4 and 8. This peculiarity will lead to a broad distribution of molecular weights in the synthesis of the final star polymer through radical polymerisation. However, as first attempt, the mixture of *p*-dodecylcalix[n]arenes was considered a good model to understand if the coupling reaction between linear polymers and the calixarene core can take place in mineral oil.

After the esterification reaction with methacryloyl chloride, it was however not easy to confirm the complete functionalisation of this compound. The ^{1}H NMR spectrum was in fact affected by very broad signals. Conceivably the removal of the intramolecular hydrogen bonds between the hydroxyl groups at the lower rim as a consequence of their acylation, causes a more conformationally mobile situation for the macrocycles. Moreover, the great variability at the upper rim contributes to enlarge the signals of the spectrum. In addition to this, compound **28**

was not soluble in the solvents used by the ESI-MS instrument so it was not possible to have a confirmation of the complete functionalisation with the mass spectrum.

IR spectroscopy could however give interesting hints. *Figure 56* shows the IR spectrum of compound **28** on the top and of the mixture of *p*-dodecylcalix[n]arenes on the bottom. In the spectrum of **28** at 1743.7 cm^{-1} it is possible to observe the peak of absorption relative to the stretching mode of the ester C=O group at the lower rim of the calixarenes, while the peak at 1465.5 cm^{-1} belongs to the stretching of the methacrylate C=C double bond. Moreover, if the two spectra are compared is possible to observe the complete disappearance of the broad signal of the hydroxyl groups at 3181.4 cm^{-1}. It seems therefore highly probable that the complete functionalisation of the macrocycles was achieved.

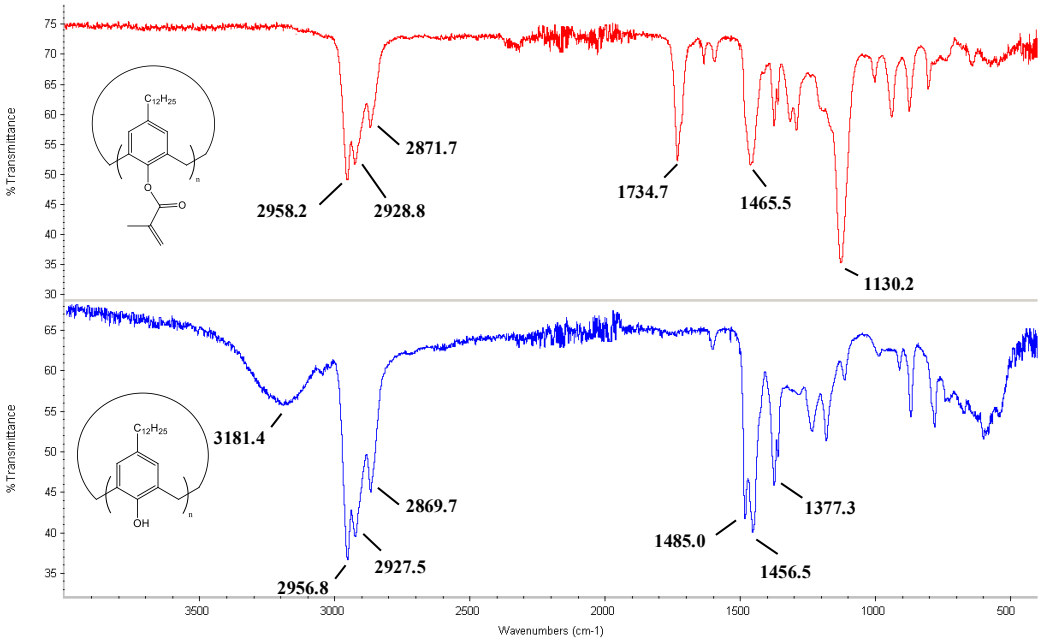


Figure 56 – On the top: IR spectrum of compound **28**. On the bottom: IR spectrum of the *p*-dodecylcalix[n]arenes.

3.7.3 Solubility test in the oil SN150

After their syntheses, it was necessary to verify the solubility in mineral oil of the last two products. Two solutions of the two compounds at 5% w/w in SN 150S were prepared, the mixtures were heated at 60°C and mixed for about one hour. At the end the two solutions were cooled to room temperature and let it rest for another hour.

The solution of compound **27** appeared cloudy and on the bottom of the round flask was present a great amount of precipitate. On the other hand, the solution of **28** was clear and the calixarene derivative was completely soluble in mineral oil. For these reasons only compound **28** was sent to the research group of Prof. Laus to study the formation of the star polymer.

In the next future derivative **28** will be studied in coupling reaction with the polymeric chains grown by radical polymerisation in mineral oil.

3.8 Conclusion

The aim of the research activity described in this chapter was to explore the potentiality of calixarene scaffolds as core for the synthesis and development of star polymers, exploiting the so-called arm-first approach.

Exploiting the Living Anionic Polymerisation and starting from compound **2**, it was obtained a styrene-butadiene star copolymer that was purified and its properties as Viscosity Index Improver (VII) were evaluated. It was established that, with such star architecture obtained

from a calixarene core, it is possible to increase the viscosity of the oil and to also reach a good mechanical shear stability.

In the following investigations, new derivatives of the central calixarene core were proposed and synthesised to solve the problems of steric hindrance encountered in the coupling with styrene-butadiene anionic copolymer, and of decoupling during the hydrogenation step. The benzyl ether bond present in compound **2** was therefore removed and the linker connecting the ester moiety to the central core was significantly elongated. It was also studied the insertion of epoxide moieties as a possible functional group for the coupling reaction between calixarenes and the linear polymers grown by living anionic polymerisation. Due to a very critical issue related to the elimination of the epoxide groups under the highly basic condition of living anionic polymerisation, it was however not possible to implement the epoxide as a reactive unit for the preparation of these type of star polymers. However, these studies offers some novel and successful insights for the introduction of electrophilic groups at the lower rim of the *p*-*tert*-butylcalix[8]arene.

In the second part of the chapter, it was synthesised a small library of calixarenes potentially able to react with polymer chains generated by radical polymerisation These calixarenes have also to be soluble in the mineral oil that is the reaction media industrially exploited for such synthetic processes. The only product of the library that results soluble in oil is the derivative **28**, based on a mixture of *p*-dodecylcalix[n]arenes (n = 4-8). These findings suggest that, for a fair solubility in mineral oil, any macrocycle must be provide of long and branched chains and that the simple functionalisation of the hydroxyl groups is not sufficient to

guarantee this solubility. In the next future, product **28** will be tested in the synthesis of star polymer within a collaboration with the research group of Prof. Michele Laus at the University of "Piemonte Orientale".

3.9 Experimental Section

General Information: All moisture sensitive reactions were carried out under nitrogen atmosphere, using previously oven-dried glassware. All dry solvents were prepared according to standard procedures, distilled before use and stored over 3 or 4 Å molecular sieves. Most of the solvents and reagents were obtained from commercial sources and used without further purification. Analytical TLC were performed using prepared plates of silica gel (Merck 60 F-254 on aluminum) and then, according to the functional groups present on the molecules, revealed with UV light or using staining reagents: $FeCl_3$ (1% in H_2O/CH_3OH 1:1), H_2SO_4 (5% in EtOH), ninhydrin (5% in EtOH), basic solution of $KMnO_4$ (0.75% in H_2O). Reverse phase TLC were performed by using silica gel 60 RP-18 F-254 on aluminum sheets. Merck silica gel 60 (70-230 mesh) was used for flash chromatography and for preparative TLC plates. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AV300 and Bruker AV400 spectrometers (observation of ^1H nucleus at 300 MHz and 400 MHz respectively, and of ^{13}C nucleus at 75 MHz and 100 MHz respectively). All chemical shifts are reported in part per million (ppm) using the residual peak of the deuterated solvent, which values are referred to tetramethylsilane (TMS, $\delta = 0$), as internal standard. All ^{13}C NMR spectra were performed with proton decoupling. Electrospray ionisation (ESI) mass analyses were performed with a Waters spectrometer. Atmospheric pressure photoionisation (APPI) mass analysis were performed with an Agilent 1100 series LC MSD TRAP. Melting points were determined on an Electrothermal apparatus in closed capillaries.

5,11,17,23,29,35,41,47-octa-*tert*-butyl-49,50,51,52,53-54,55,56-octa (*p*-(methyloxycarbonyl)-benzyloxycalix[8]arene (2)

To a 250 ml round bottom flask, *p-tert*-butylcalix[8]arene (8.24 g, 50.84 mmol), potassium carbonate (13.25 g, 95.93 mmol), potassium iodide (1.03 g, 6.19 mmol) and methyl 4-(bromomethyl)benzoate (16.45 g, 71.82 mmol) were dissolved in acetone (60 mL) and toluene (40 mL). The mixture was stirred at reflux for two days. The reaction was monitored by TLC (hexane : EtOAc = 8:2). At total consumption of the reagent, the suspension was filtered and then solvent was removed under reduced pressure to give a yellow solid. The solid was dissolved in EtOAc (200 ml) and washed with 1 M HCl (2x100ml). The organic phase was separated, dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by precipitation in MeOH to give **2** as a white solid (8.10 g, 51.3%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.75 (d, J = 8.2 Hz, 16H, H_{Ar}); 7.14 (d, J = 8.2 Hz, 16H, H_{Ar}); 6.94 (s, 16H, H_{Ar}); 4.55 (s, 16H, OCH_2); 3.98 (s, 16H, ArCH_2Ar); 3.90 (s, 24H, CO_2CH_3); 0.98 (s, 72H, C(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.9 (*C*O); 152.8 (C_{Ar}); 146.4 (C_{Ar}); 142.8 (C_{Ar}); 133.0 (C_{Ar}); 129.6 (C_{Ar}); 129.2 (C_{Ar}); 126.8 (C_{Ar}); 126.2 (C_{Ar}); 73.9 (OCH_2); 52.1 (CO_2CH_3); 34.2 (Ar*C*H$_2$Ar); 31.4 (C(*C*H$_3$)$_3$); 30.3 (*C*(CH$_3$)$_3$).

Compound **3**

To a 100 ml round bottom flask, derivative **2** (0.1 g, 0.04 mmol), 10 ml of dry cyclohexane and 10 μl of dry THF were added. The solution was mixed and heated at 40°C for 15 minutes. Then, 0.04 ml of *n*-BuLi (solution of 1.6 M in hexane) were added dropwise. The mixture was

stirred at 40°C for 20 minutes. At the end EtOAc (20 ml) and 1M HCl (20 ml) were added. The organic phase was separated, washed with distilled water (2x10 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give **3** as a yellow oil (115 mg, 92.8%). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ (ppm): 7.70-6.70 (m, 48H, H_{Ar}); 4.75 (s, 16H, OCH_2); 4.12 (s, 16H, ArCH_2Ar); 3.55 (bs, 8H, OH); 2.03-0.54 (m, 216H, C(CH_3)$_3$, CH_2CH_2CH_2CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$) δ (ppm): 153.1 (C_{Ar}); 146.8 (C_{Ar}); 145.8 (C_{Ar}); 135.5 (C_{Ar}); 133.4 (C_{Ar}); 127.4 (C_{Ar}); 126.1 (C_{Ar}); 125.5 (C_{Ar}); 75.9 (OCH_2); 74.4 (CH$_2$*C*OH); 43.3 (CH_2CH$_2$CH$_2$CH$_3$); 34.2 (Ar*C*H$_2$Ar); 31.4 (C(*C*H$_3$)$_3$); 30.3 (*C*(CH$_3$)$_3$); 25.6 (CH$_2$CH_2CH$_2$CH$_3$); 23.1 (CH$_2$CH$_2$CH_2CH$_3$); 13.7 (CH_2CH$_2$CH$_2$CH_3).

1-(*tert*-butyl)-4-(prop-2-yn-1-yloxy)benzene (4)

4 was synthesised according to a literature procedure.[25] To a 100 ml round-bottom flask, *p-tert*-butylphenol (2.33 g, 15.57 mmol), potassium carbonate (4.30 g, 31.14 mmol) and 20 ml of acetone were added. The suspension was stirred for 20 minutes then propargyl bromide (0.98 ml, 11.98 mmol) was added via syringe at room temperature. The reaction mixture was heated at 70°C and stirred for 18 hours. The reaction was monitored by TLC (toluene : EtOAc = 9.5:0.5). At total consumption of the reagent, the reaction was cooled to room temperature. dichloromethane (50 ml) and 1M HCl (50 ml) were added, then the organic phase was separated, washed with brine (2x30 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure to give **4** as an orange oil (2.60 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$)

δ (ppm): 7.35 (d, J = 8.8 Hz, 2H, H_{Ar}); 6.95 (d, J = 8.8 Hz, 2H, H_{Ar}); 4.70 (d, J = 2.4 Hz, 2H, OCH_2CCH); 2.54 (t, J = 2.4 Hz, 1H, OCH_2CCH); 1.33 (s, 9H, $C(CH_3)_3$). The ^{13}C NMR and ESI-MS data are in agreement with those reported in literature.[25]

Methyl 4-(3-(4-(*tert*-butyl)phenoxy)prop-1-yn-1-yl)benzoate (6)

To a 100 ml round-bottom flask, **4** (0.41 g, 2.16 mmol), diisopropylamine (3.5 ml, 24.97 mmol), tetrakis(triphenylphosphine)palladium(0) **(**0.05 g, 0.04 mmol), copper(I) iodide (0.023 g, 0.09 mmol), methyl 4-bromobenzoate (0.55 g, 2.26 mmol) and 7 ml of toluene were added. The reaction mixture was heated to 110°C and stirred for 18 hours. The reaction was monitored by TLC (hexane : dichloromethane = 6:4). At total consumption of the reagent, the reaction was cooled to room temperature. EtOAc (40 ml) and brine (40 ml) were added, then the organic phase was separated, washed with brine (2x30 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane : EtOAc = 99:1) to give **6** as a yellow solid (0.09 g, 11%). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, J = 8.4 Hz, 2H, H_{Ar}); 7.53 (d, J = 8.4 Hz, 2H, H_{Ar}); 7.37 (d, J = 8.8 Hz, 2H, H_{Ar}); 6.99 (d, J = 8.8 Hz, 2H, H_{Ar}); 4.93 (s, 2H, OCH_2); 3.94 (s, 3H, CO_2CH_3); 1.34 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.4 (CO_2CH_3); 155.5 (C_{Ar}); 144.3 (C_{Ar}); 131.7 (C_{Ar}); 129.9 (C_{Ar}); 129.4 (C_{Ar}); 127.0 (C_{Ar}); 126.3 (C_{Ar}); 114.4 (C_{Ar}); 87.2 (OCH_2CCAr); 86.1 (OCH_2CCAr); 56.6 (OCH_2CCAr); 52.2 (CO_2CH_3); 34.1 ($C(CH_3)_3$); 31.5 ($C(CH_3)_3$).

5,11,17,23,29,35,41,47-octa-*tert*-butyl-49,50,51,52,53-54,55,56-octapropargyloxycalix[8]arene (7)

To a 100 ml round-bottom flask, *p-tert*-butylcalix[8]arene (1.29 g, 0.99 mmol), potassium carbonate (2.18 g, 15.84 mmol) and 50 ml of acetone were added. The suspension was stirred for 20 minutes then propargyl bromide (0.98 ml, 11.98 mmol) was added via syringe at room temperature. The reaction mixture was heated at 70°C and stirred for 18 hours. The reaction was monitored by TLC (hexane : EtOAc = 8:2). At total consumption of the reagent, the reaction was cooled to room temperature and dichloromethane (100 ml) and 1M HCl (100 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by crystallisation from dichloromethane/MeOH to give **7** as a white powder (1.49 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.97 (s, 16H, H_{Ar}); 4.23 (d, J = 2.3 Hz, 16H, OCH_2CCH); 4.12 (s, 16H, ArCH_2Ar); 2.31 (t, J = 2.3 Hz, 8H, OCH$_2$CC*H*); 1.13 (s, 72H, C(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 152.9 (C_{Ar}); 146.7 (C_{Ar}); 133.2 (C_{Ar}); 126.1 (C_{Ar}); 79.5 (OCH$_2$*C*CH); 75.2 (OCH$_2$C*C*H); 60.7 (O*C*H$_2$CCH); 34.2 (Ar*C*H$_2$Ar); 31.4 (C(*C*H$_3$)$_3$); 31.0 (*C*(CH$_3$)$_3$). ESI-MS: Mass calcd for $C_{112}H_{128}O_8$: 1602.21 Found: m/z 1625.87 [100%, $(M+Na)^+$]; 1641.56 [40%, $(M+K)^+$]. M.p.: 130-131°C dec.

Methyl 4-(azidomethyl)benzoate (10)

10 was synthesised according to a literature procedure.[10,11] To a 250 ml round-bottom flask, methyl (4-bromomethyl)benzoate (8.27 g,

33.43 mmol), 115 ml of acetone and 35 ml of distilled water were added. NaN_3 (8.95 g, 133.75 mmol) was added carefully to the solution under vigorous stirring. The reaction mixture was heated at 70°C and stirred for 18 hours. The reaction was monitored by TLC (hexane : EtOAc = 9.5:0.5). At total consumption of the reagent, the reaction was cooled to room temperature and EtOAc (130 ml) and 1M HCl (130 ml) were added. The organic phase was separated, washed with brine (3x100 ml), dried over anhydrous Na_2SO_4 and concentrated in vacuo to yield a yellow oil (6.4 g, 95%). The product was used for the next reaction without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.07 (d, J = 8.0 Hz, 2H, H_{Ar}); 7.40 (d, J = 8.0 Hz, 2H, H_{Ar}); 4.43 (s, 2H, N_3CH_2); 3.94 (s, 3H, CO_2CH_3). The ^{13}C NMR and ESI-MS data are in agreement with those reported in literature.

Methyl 4-((4-((4-*tert*-butylphenoxy)methyl)-1H-1,2,3-triazol-1yl) methyl)benzoate (11)

4 (0.36 g, 1.78 mmol), 7 ml of DMF, 10 drops of distilled water, **10** (0.112 g, 0.60 mmol), $CuSO_4$•$5H_2O$ (0.062 g, 0.18 mmol) and (+)-sodium L-ascorbate (0.07 g, 0.36 mmol) were added to a 10 ml MW-vial equipped with a magnetic stirrer. The mixture was subjected to MW irradiation with gas cooling and magnetic stirring for 1 hour at 150W and a temperature limit of 80°C, for two cycles, monitoring the reaction with TLC (hexane : EtOAc : MeOH = 7:2.5:0.5). At total consumption of the reagent EtOAc (15 ml) and distilled water (15 ml) were added. The organic phase was separated, washed with distilled water (2x15 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under

reduced pressure. The crude was purified by flash chromatography (hexane : EtOAc : MeOH = 8:1.5:0.5 → 7:2.5:0.5) to give **11** as a white solid (0.16 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.06 (d, J = 8.4 Hz, 2H, H_{Ar}); 7.57 (s, 1H, CC*H*N); 7.34-7.30 (m, 4H, H_{Ar}); 6.92 (d, J = 8.8 Hz, 2H, H_{Ar}); 5.61 (s, 2H, NCH_2Ar); 5.21 (s, 2H, OCH_2); 3.94 (s, 3H, CO_2CH_3); 1.31 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.4 (CO_2CH_3); 155.9 (C_{Ar}); 145.3 (C_{Ar}); 144.0 (*C*CHN); 139.3 (C_{Ar}); 130.6 (C_{Ar}); 130.4 (C_{Ar}); 127.8 (C_{Ar}); 126.3 (C_{Ar}); 122.6 (C*C*HN); 114.2 (C_{Ar}); 62.2 (O*C*H$_2$); 53.7 (N*C*H$_2$Ar); 52.3 (CO_2CH_3); 34.1 (*C*(CH$_3$)$_3$); 31.5 (C(*C*H$_3$)$_3$). ESI-MS: Mass calcd for $C_{22}H_{25}N_3O_3$: 379.45 Found: m/z 380.44 [20%, $(M+H)^+$]; 402.40 [100%, $(M+Na)^+$]; 419.32 [20%, $(M+K)^+$]; 781.50 [100%, $(2M+Na)^+$]; 797.48 [10%, $(2M+K)^+$]; 1160.52 [10%, $(3M+Na)^+$].

Compound **12**

7 (1.37 g, 1.85 mmol), 20 ml of DMF, 20 drops of distilled water, **10** (2.06 g, 10.26 mmol), $CuSO_4$•$5H_2O$ (0.51 g, 2.97 mmol) and (+)-sodium L-ascorbate (0.81 g, 4.01 mmol) were added to a 50 ml MW-vial equipped with a magnetic stirrer. The mixture was subjected to MW irradiation with gas cooling and magnetic stirring for 2 hours at 150W and a temperature limit of 80°C, for three cycles, monitoring the reaction by TLC (hexane : EtOAc : MeOH = 5:4:1). At total consumption of the reagent EtOAc (100 ml) and distilled water (100 ml) were added. The organic phase was separated, washed with brine (2x100 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude was heated in hot EtOAc and after cooling to room

temperature, the product was collected by vacuum filtration to give **12** as a brown solid (1.82 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.86 (d, J = 8.0 Hz, 16H, H_{Ar}); 7.85 (s, 8H, CC*H*N); 7.16 (d, J = 8.0 Hz, 16H, H_{Ar}); 6.86 (s, 16H, H_{Ar}); 5.32 (s, 16H, NCH_2Ar); 4.73 (s, 16H, OCH_2); 4.05 (bs, 16H, ArCH_2Ar); 3.88 (s, 24H, CO_2CH_3); 0.96 (s, 72H, C(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.3 (CO_2CH_3); 152.4 (C_{Ar}); 146.5 (C_{Ar}); 144.5 (*C*CHN); 139.9 (C_{Ar}), 132.9 (C_{Ar}); 130.1 (C_{Ar}); 127.8 (C_{Ar}); 125.9 (C_{Ar}); 124.1 (C*C*HN); 66.4 (O*C*H$_2$); 53.2 (N*C*H$_2$Ar); 52.2 (CO_2CH_3); 34.1 (*C*(CH_3)$_3$); 31.2 (C(*C*H$_3$)$_3$); 29.8 (Ar*C*H$_2$Ar). ESI-MS: Mass calcd for $C_{184}H_{200}N_{24}O_{24}$: 3129.51 Found: m/z 779.83 [100%, $(M+4H)^{4+}$]. M.p.: 229-231°C dec.

4-*tert*-butylphenyl glycidyl ether (13)

To a 100 ml round-bottom flask, *p-tert*-butylphenol (1.20 g, 7.98 mmol), potassium *tert*-butoxide (0.98 g, 8.78 mmol) and 30 ml of acetonitrile were added. The mixture was stirred for 20 minutes, then epichlorohydrin (2.05 ml, 18.51 mmol) was added carefully. The reaction mixture was heated to 95°C and stirred for 18 hours. The reaction was monitored by TLC (toluene : EtOAc = 9:1). At total consumption of the reagent, EtOAc (100 ml) and brine (100 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give **13** as a yellow oil (1.49 g, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.32 (d, J = 9.0 Hz, 2H, H_{Ar}); 6.88 (d, J = 9.0 Hz, 2H, H_{Ar}); 4.21 (dd, J_1 = 3.3 Hz, J_2 = 11.1 Hz, 1H, OC*H*HCHOCH$_2$); 4.00 (dd, J_1 = 5.4 Hz, J_2 = 11.1 Hz, 1H, OCH*H*CHOCH$_2$); 3.40-3.35 (m, 1H, OCH2C*H*OCH$_2$); 2.92 (t, J = 4.2

Hz, 1H, $OCH_2CHOCHH$); 2.77 (dd, J_1 = 2.7 Hz, J_2 = 4.8, 1H, $OCH_2CHOCHH$); 1.32 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 157.0 (C_{Ar}); 145.3 (C_{Ar}); 126.3 (C_{Ar}); 114.0 (C_{Ar}); 68.7 (OCH_2CHOCH_2); 50.2 (OCH_2CHOCH_2); 44.8 (OCH_2CHOCH_2); 34.6 ($C(CH_3)_3$); 31.5 ($C(CH_3)_3$). ESI-MS: Mass calcd for $C_{13}H_{18}O_2$: 206.13 Found: m/z 435.60 [100%, $(2M+Na)^+$]; 451.50 [10%, $(2M+K)^+$].

Other procedure to **13**

To a 50 ml round-bottom flask, **14** (1.09 g, 5.77 mmol) was dissolved in 30 ml of dry dichloromethane. The mixture was cooled down to 0°C, then 3-chloroperbenzoic acid 77% w/w (2.0 g, 8.65 mmol) was added over a period of 30 minutes. The reaction mixture was stirred at 0°C for 30 minutes, then it was stirred at room temperature for 15 hours. The reaction was monitored by TLC (toluene). At total consumption of the reagent, EtOAc (100 ml) and sodium bicarbonate solution at 5% (100 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane : EtOAc = 9.5:0.5) to give **13** as a yellow oil (0.38 g, 39%).

Allyl 4-*tert*-butylphenyl ether (14)

To a 100 ml round-bottom flask, *p*-*tert*-butylphenol (2.78 g, 7.98 mmol), potassium carbonate (7.41 g, 53.65 mmol) and 100 ml of acetone were added. The mixture was stirred for 20 minutes then allyl bromide (2.05 ml, 18.51 mmol) and potassium iodide in catalytic amount (0.685 g, 4.12 mmol) were added. The reaction mixture was heated at 70°C for 18

hours and it was monitored by TLC (hexane : toluene = 2:8). At total consumption of the reagent, EtOAc (100 ml) and 1M HCl (100 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give **14** as a yellow oil (6.63 g, 84%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.30 (d, J = 8.8 Hz, 2H, H_{Ar}); 6.97 (d, J = 8.8 Hz, 2H, H_{Ar}); 6.20-6.11 (m, 1H, OCH_2CHCH_2); 5.51 (dd, J_1 = 1.6 Hz, J_2 = 17.2 Hz, 1H, OCH_2CHCHH); 5.37 (dd, J_1 = 1.6 Hz, J_2 = 10.4 Hz, 1H, OCH_2CHCHH); 4.61 (dt, J_1 = 1.4 Hz, J_2 = 5.3 Hz, 2H, OCH_2CHCH_2); 1.41 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 156.5 (C_{Ar}); 143.5 (C_{Ar}); 133.7 (OCH_2CHCH_2); 126.2 (C_{Ar}); 117.5 (OCH_2CHCH_2); 114.3 (C_{Ar}); 68.9 (OCH_2CHCH_2); 34.1 ($C(CH_3)_3$); 31.6 ($C(CH_3)_3$).

5,11,17,23,29,35,41-octa-*tert*-butyl-49,50,51,52,53,54,55,56 octaallyloxycalix[8]arene (15)

15 was synthesised according to a literature procedure.[26] To a 100 ml round-bottom flask, *p-tert*-butylcalix[8]arene (1.30 g, 1.0 mmol), potassium hydroxide (0.67 g, 12.0 mmol) in 20 ml of distilled water, PEG400 (5 g), allyl bromide (2.9 g, 24.0 mmol) and 20 ml of Chloroform were added. The mixture was stirred for 20 hours at room temperature. The reaction was monitored by TLC (hexane : EtOAc = 9:1). At total consumption of the reagent, dichloromethane (30 ml) and 1M HCl (30 ml) were added. The organic phase was separated, washed with 1M HCl (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by crystallisation DCM/MeOH to give **15** as a yellow powder (1.16 g, 89%). ^{1}H NMR

(400 MHz, $CDCl_3$) δ (ppm): 6.98 (s, 16H, H_{Ar}); 5.80-5.72 (m, 8H, CH_2CHCH_2); 5.05 (d, J = 17.2 Hz, 8H, OCH_2CHCHH); 4.90 (d, J = 10 Hz, 8H, OCH_2CHCHH); 4.05 (s, 16H, $ArCH_2Ar$); 3.99 (d, J = 4.0 Hz, 16H, OCH_2CHCH_2); 1.20 (s, 72H, $C(CH_3)_3$). The ^{13}C NMR and ESI-MS data are in agreement with those reported in literature.[26]

5,11,17,23,29,35,41-octa-*tert*-butyl-49,50,51,52,53,54,55,56 octaglycidoxycalix[8]arene (16)

To a two-neck 50 ml round-bottom flask, equipped with a nitrogen source, **15** (0.20 g, 0.12 mmol) was dissolved in 30 ml of dry dichloromethane. The mixture was cooled down to 0°C, then 3-chloroperbenzoic acid 77% w/w (0.37 g, 1.50 mmol) was added over a period of 30 minutes. The reaction mixture was stirred at 0°C for 30 minutes, then it was stirred at room temperature for 15 hours. The reaction was monitored by TLC (toluene : EtOAc = 9.5:0.5). At total consumption of the reagent, dichloromethane (100 ml) and sodium bicarbonate solution at 5% (100 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by crystallisation from DCM/Et_2O to give **16** as a white powder (0.04 g, 18%). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.98 (s, 16H, H_{Ar}); 4.03 (s, 16H, $ArCH_2Ar$); 3.79 (m, 8H, $OCHHCHOCH_2$); 3.59 (m, 8H, $OCHHCHOCH_2$); 3.11 (m, 8H, OCH_2CHOCH_2); 2.48 (s, 8H, $OCH_2CHOCHH$); 2.37 (s, 8H, $OCH_2CHOCHH$); 1.13 (s, 72H, $C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 152.8 (C_{Ar}); 146.3 (C_{Ar}); 132.9

(C_{Ar}); 125.9 (C_{Ar}); 73.7 (OCH_2CHOCH_2); 50.3 (OCH_2CHOCH_2); 44.2 (OCH_2CHOCH_2); 34.2 ($ArCH_2Ar$); 31.3 ($C(CH_3)_3$); 31.0 ($C(CH_3)_3$).

Ethyl 2-(4-*tert*-butylphenoxy)acetate (20)

To a 100 ml round-bottom flask, *p-tert*-butylphenol (2.78 g, 7.98 mmol), potassium carbonate (3.57 g, 25.91 mmol) and 50 ml of acetone were added. The mixture was stirred for 20 minutes then ethyl bromoacetate (2.05 ml, 18.51 mmol) was added carefully. The reaction mixture was heated at 70°C and stirred for 18 hours. The reaction was monitored by TLC (toluene : EtOAc = 9:1). At total consumption of the reagent, EtOAc (30 ml) and 1M HCl (30 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give **20** as a yellow oil (3.92 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.33 (d, J = 8.8 Hz, 2H, H_{Ar}); 6.87 (d, J = 8.8 Hz, 2H, H_{Ar}); 4.62 (s, 2H, OCH_2CO_2); 4.29 (q, J = 7.2 Hz, 2H, CH_2CH_3); 1.34-1.30 (m, 12H, CH_2CH_3, $C(CH_3)_3$). The ^{13}C NMR and ESI-MS data are in agreement with those reported in literature.[27]

2-(4-*tert*-butylphenoxy)ethanol (21)

To a 100 ml three-neck round-bottom flask equipped with a dropping funnel and a thermometer, **20** (0.65 g, 2.79 mmol) was dissolved in 16 ml of dry THF and the solution was cooled down to 0°C. $LiAlH_4$ (0.32 g, 8.40 mmol) was dissolved in 15 ml of dry THF and it was added carefully to the solution dropwise over a period of 30 minutes. The reaction mixture was stirred at room temperature for 18 hours and it was monitored by

TLC (toluene : EtOAc = 9:1). At total consumption of the reagent, the excess of reductant was destroyed by adding 7 ml of 1M HCl. Then, EtOAc (30 ml) and 1M HCl (30 ml) were added. The organic phase was separated, washed with distilled water (2x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give **21** as a colourless oil (0.48 g, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.35 (d, J = 8.8 Hz, 2H, H_{Ar}); 6.90 (d, J = 8.8 Hz, 2H, H_{Ar}); 4.10 (t, J = 4.1 Hz, 2H, OCH_2CH_2OH); 3.98 (t, J = 4.1 Hz, 2H, OCH_2CH_2OH); 3.40 (bs, 1H, OCH_2CH_2OH); 1.35 (s, 9H, $C(CH_3)_3$). The ^{13}C NMR and ESI-MS data are in agreement with those reported in literature.[28]

2-((2-(4-(*tert*-butyl)phenoxy)ethoxy)methyl)oxirane (22)

To a 100 ml round-bottom flask, **21** (0.158 g, 0.81 mmol), potassium *tert*-butoxide (0.118 g, 1.05 mmol) and 7 ml of acetonitrile were added. The mixture was stirred for 20 minutes, then epichlorohydrin (0.11 g, 1.21 mmol) was added carefully. The reaction mixture was heated at 95°C and it was monitored by TLC (toluene : EtOAc = 95:5). After 72 hours it wasn't reached the total consumption of the reagent, so EtOAc (100 ml) and brine (100 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced. Product **22** was separated from the unreacted **21** by flash chromatography (hexane : EtOAc = 9:1). **22** appears as a colourless oil (0.1 g, 47%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.33 (d, J = 8.7 Hz, 2H, H_{Ar}); 6.89 (d, J = 8.7 Hz, 2H, H_{Ar}); 4.15 (t, J = 10.7 Hz, 2H, OCH_2CH_2O); 3.92-3.86 (m, 3H, OCH_2CH_2O, $OCHHCHOCH_2$); 3.52 (dd, J_1 = 5.8 Hz, J_2 = 11.6 Hz, 1H,

OCH*H*CHOCH$_2$); 3.23-3.18 (m, 1H, OCH$_2$C*H*OCH$_2$); 2.82 (t, J = 5.0 Hz, 1H, OCH$_2$CHOC*H*H); 2.65 (dd, J_1 = 2.7 Hz, J_2 = 5.0, 1H, OCH$_2$CHOCH*H*); 1.33 (s, 9H, C(C*H*$_3$)$_3$). ^{13}C NMR (75 MHz, CDCl$_3$) δ (ppm): 156.5 (*C*$_{Ar}$); 143.6 (*C*$_{Ar}$); 126.2 (*C*$_{Ar}$); 114.1 (*C*$_{Ar}$); 72.0 (O*C*H$_2$CHOCH$_2$); 70.0 (O*C*H$_2$CH$_2$O); 67.4 (OCH$_2$*C*H$_2$O); 50.8 (OCH$_2$*C*HOCH$_2$); 44.2 (OCH$_2$CHO*C*H$_2$); 34.0 (*C*(CH$_3$)$_3$); 31.5 (C(*C*H$_3$)$_3$). ESI-MS: Mass calcd for C$_{15}$H$_{22}$O$_3$: 250.16 Found: m/z 273.42 [100%, (M+Na)$^+$]; 289.42 [20%, (M+K)$^+$].

Methyl (4-azidomethyl)styrene (23)

23 was synthesised according to a literature procedure.[20] To a 100 ml round-bottom flask, 4-vynilbenzyl chloride (0.92 ml, 5.55 mmol), 35 ml of acetone and 5 ml of distilled water were added. NaN_3 (2.12 g, 32.75 mmol) was added carefully to the solution under vigorous stirring. The reaction mixture was stirred at room temperature for 18 hours. The reaction was monitored by TLC (hexane : EtOAc = 9.5:0.5). At total consumption of the reagent, the reaction was cooled to room temperature and toluene (30 ml) and distilled water (30 ml) were added. The organic phase was separated, washed with distilled water (2x20 ml), dried over anhydrous Na_2SO_4 and concentrated in vacuo to yield a yellow oil (0.99 g, 96%). The product was used for the next reaction without further purification. ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 7.45 (d, J = 8.1 Hz, 2H, H$_{Ar}$); 7.31 (d, J = 8.1 Hz, 2H, H$_{Ar}$); 6.80-6.71 (dd, J_1 = 10.8 Hz, J_2 = 17.7 Hz, 1H, ArC*H*CH$_2$); 5.83-5.77 (dd, J_1 = 0.6 Hz, J_2 = 17.7 Hz, 1H, ArCHC*H*H); 5.33-5.29 (dd, J_1 = 0.6 Hz, J_2 = 11.1 Hz, 1H, ArCHCH*H*);

4.35 (s, 2H, N_3CH_2). The ^{13}C NMR and ESI-MS data are in agreement with those reported in literature.[20]

Derivative **24**

7 (1.66 g, 1.04 mmol), 20 ml of dry DMF, 20 drops of distilled water, **23** (1.98 g, 12.49 mmol), $CuSO_4 \bullet 5H_2O$ (0.62 g, 2.49 mmol) and (+)-sodium L-ascorbate (0.98 g, 5.0 mmol) were added to a 50 ml MW-vial equipped with a magnetic stirrer. The mixture was subjected to MW irradiation with gas cooling and magnetic stirring for 2 hours at 150W and a temperature limit of 80°C, for three cycles, monitoring the reaction with TLC (hexane : EtOAc : MeOH = 6:3.5:0.5). At total consumption of the reagent EtOAc (150 ml) and brine (150 ml) were added. The organic phase was separated, washed with brine (2x100 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude products were purified by crystallisation from DCM/MeOH to give **24** as a brown powder (1.07 g, 36%). ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.71 (s, 8H, CC*H*N); 7.20 (d, J = 8.0 Hz, 16H, H_{Ar}); 7.06 (d, J = 8.0 Hz, 16H, H_{Ar}); 6.86 (s, 16H, H_{Ar}); 6.64-6.54 (dd, J_1 = 10.8 Hz, J_2 = 17.7 Hz, 8H, ArC*H*CH_2); 5.69-5.63 (dd, J_1 = 0.6 Hz, J_2 = 17.7 Hz, 8H, ArCHC*H*H); 5.33-5.29 (m, 24H, ArCHCH*H*, OCH_2); 4.71 (s, 16H, NCH_2Ar); 4.03 (sb, 16H, ArCH_2Ar); 0.94 (s, 72H, C(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 152.5 (C_{Ar}); 146.4 (C_{Ar}); 144.5 (*C*CHN); 137.6 (Ar*C*HCH_2); 136.0 (C_{Ar}); 134.4 (C_{Ar}); 133.0 (C_{Ar}); 128.2 (C_{Ar}); 126.6 (C_{Ar}); 125.8 (C_{Ar}); 123.9 (C*C*HN); 114.5 (ArCH*C*H_2); 66.4 (OCH_2); 53.4 (NCH_2Ar); 34.1 (*C*(CH_3)$_3$); 31.2 (C(*C*H_3)$_3$); 29.8 (ArCH_2Ar). ESI-MS: Mass calcd for $C_{184}H_{200}N_{24}O_8$: 2873.59 Found: m/z 1470.42

[100%, $(M+H_2O+2Na)^{2+}$]; 1502.53 [100%, $(M+3H_2O+2K)^{2+}$]. M.p.: 150-152°C dec.

5,11,17,23,29,35,41,47-octa-*tert*-butyl-49,50,51,52,53-54,55,56-octaacryloyloxycalix[8]arene (25)

25 was synthesised according to a literature procedure.[21] To a 100 ml round-bottom flask, *p-tert*-butylcalix[8]arene (1 g, 0.77 mmol), triethylamine (0.94 ml, 6.78 mmol) and 15 ml of Chloroform were added. The reaction mixture was cooled down to 0°C and acryloyl chloride (0.75 ml, 9.24 mmol) was added carefully to the solution under vigorous stirring. The reaction mixture was stirred at room temperature for 48 hours. The reaction was monitored by TLC (hexane : EtOAc = 9:1). At total consumption of the reagent, dichloromethane (50 ml) and sodium bicarbonate solution (50 ml) were added. The organic phase was separated, washed with sodium bicarbonate solution (3x30 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by crystallisation from DCM/Et_2O to give **25** as a white powder (0.81 g, 24%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.99 (s, 16H, H_{Ar}); 6.23 (d, J = 17.2 Hz, 8H, OCOC*H*CH_2); 5.96 (m, 8H, OCOCHC*H*H); 5.61 (d, J = 9.6 Hz, 8H, OCOCHCH*H*); 3.60 (s, 16H, ArC*H*$_2$Ar); 1.18 (s, 72H, C(C*H*$_3$)$_3$). APPI-MS: Mass calcd for $C_{112}H_{128}O_{16}$: 1728.92 Found: m/z 1751.91 [100%, $(M+Na)^+$]. The ^{13}C NMR data are in agreement with those reported in literature.[21]

5,11,17,23,29,35,41,47-octa-*tert*-butyl-49,50,51,52,53-54,55,56-octamethacryloyloxycalix[8]arene (26)

To a 100 ml round-bottom flask, *p-tert*-butylcalix[8]arene (1.29 g, 0.99 mmol), triethylamine (1.21 ml, 8.71 mmol) and 15 ml of Chloroform were added. The reaction mixture was cooled down to 0°C and methacryloyl chloride (1.17 ml, 11.9 mmol) was added carefully to the solution under vigorous stirring. The reaction mixture was stirred at room temperature for 48 hours. The reaction was monitored by TLC (hexane : EtOAc = 9:1). At total consumption of the reagent, dichloromethane (50 ml) and sodium bicarbonate solution (50 ml) were added. The organic phase was separated, washed with sodium bicarbonate solution (3x30 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by crystallisation from DCM/Et_2O to give **26** as a white powder (0.68 g, 19%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.99 (s, 16H, H_{Ar}); 5.96 (s, 8H, OCOC(CH_3)C*H*H); 5.41 (s, 8H, OCOC(CH_3)CH*H*); 3.66 (s, 16H, ArCH_2Ar); 1.73 (s, 24H, OCOC(CH_3)CH_2); 1.15 (s, 72H, C(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 165.0 (*C*O); 148.1 (C_{Ar}); 145.3 (C_{Ar}); 135.1 (OCO*C*(CH_3)CH_2); 131.2 (C_{Ar}); 127.1 (OCOC(CH_3)*C*H_2); 126.0 (C_{Ar}); 34.3 (*C*(CH_3)$_3$); 31.2 (C(*C*H_3)$_3$); 31.2 (Ar*C*H_2Ar); 18.3 (OCOC(*C*H_3)CH_2). APPI-MS: Mass calcd for $C_{120}H_{144}O_{16}$: 1841.04 Found: m/z 1864.03 [100%, $(M+Na)^+$]. M.p.: 250-252°C.

5,11,17,23,29,35,41,47-octa-octyl-49,50,51,52,53-54,55,56-octamethacryloyloxycalix[8]arene (27)

To a 100 ml round-bottom flask, *p-tert*-octylcalix[8]arene (14.7 g, 67.35 mmol), triethylamine (10.3 ml, 74.0 mmol) and 200 ml of Chloroform were added. The reaction mixture was cooled down to 0°C and methacryloyl chloride (13.15 ml, 134.7 mmol) was added carefully to the solution under vigorous stirring. The reaction mixture was stirred at room temperature for 48 hours. The reaction was monitored by TLC (hexane : EtOAc = 9:1). At total consumption of the reagent, dichloromethane (150 ml) and sodium bicarbonate solution (150 ml) were added. The organic phase was separated, washed with a sodium bicarbonate solution (3x70 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by crystallisation from DCM/Et_2O to give **27** as a white powder (12.3 g, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.00 (bs, 16H, H_{Ar}); 5.93 (bs, 8H, COC(CH_3)C*H*H); 5.38 (bs, 8H, COC(CH_3)CH*H*); 3.64 (bs, 16H, ArCH_2Ar); 1.75 (bs, 24H, COC(CH_3)CH_2); 1.62 (bs, 16H, C(CH_3)$_2$CH_2C(CH_3)$_3$); 1.22 (bs, 48H, C(CH_3)$_2$$CH_2$C($CH_3$)$_3$); 0.73 (bs, 72H, C($CH_3$)$_2$$CH_2$C(C$H_3$)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 165.0 (*C*O); 147.4 (C_{Ar}); 145.1 (C_{Ar}); 135.2 (CO*C*(CH_3)CH_2); 131.0 (C_{Ar}); 126.8 (C_{Ar},COC(CH_3)*C*H_2); 56.7 (C_8H_{17}); 38.3 (C_8H_{17}); 32.4 (C_8H_{17}); 32.0 (C_8H_{17}); 31.5 (Ar*C*H_2Ar); 18.3 (COC(*C*H_3)CH_2). M.p.: 284-285°C.

Derivative **28**

To a 100 ml round-bottom flask, *p*-dodecylcalix[8,7,6,5,4]arene (1.4 g, 5.12 mmol), triethylamine (0.8 ml, 5.64 mmol) and 40 ml of Chloroform

were added. The reaction mixture was cooled down to 0°C and methacryloyl chloride (1.0 ml, 10.25 mmol) was added carefully to the solution under vigorous stirring. The reaction mixture was stirred at room temperature for 48 hours. The reaction was monitored by TLC (hexane : EtOAc = 9:1). At total consumption of the reagent, dichloromethane (70 ml) and sodium bicarbonate solution (70 ml) were added. The organic phase was separated, washed with a sodium bicarbonate solution (3x40 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure to give **28** as a brown oil (0.98 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.00 (bs, 16H, H_{Ar}); 6.20 (bs, 8H, COC(CH_3)C*H*H); 5.64 (bs, 8H, COC(CH_3)CH*H*); 3.74 (bs, 16H, ArCH_2Ar); 1.90-0.5 (m, 224H, COC(CH_3)CH_2, $C_{12}H_{25}$).

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Chapter 4

Calixarene Overbased Detergents

4.1 Introduction

A lubricant has to manage different types of functions, among which one of the most important is to keep the engine clean. This expression means that it has to neutralise species that can lead to degradation processes of the mechanical parts or also of the lubricant and to keep in solution carbonious particles that are generated during the combustion.

As already explained in paragraph *1.2.2*, detergents are the class of additives responsible of these tasks. They neutralise the acids formed during combustion, reduce deposits and thereby prevent sticking of piston rings.

The Total Base Number (TBN) is one of the main indexes used to characterise a detergent and reflects their ability to neutralise acids. In additives and formulated lubricants, it is expressed as the amount of KOH(mg)/g of additive. The TBN number is monitored for engine oils,

and a reduction in the TBN is a clear indication that the engine oil has to be changed.

Detergents are generally organic metal salts soluble in oil and produced by reacting a metal (generally an alkali/alkaline earth metal) base with an organic acid. The process of generation of the detergent is therefore a salification reaction of the type:

$$MOH + R\text{-}COH \rightarrow R\text{-}CO^{-}\ M^{+} + H_2O$$

If the base and the organic acid are added in stoichiometric proportions, the oil soluble alkaline earth metal salt is considered to be neutral. If, on the other hand, the base is added in excess (compared to the amount of organic acid) the detergent is denoted as *overbased*.

Overbased detergents are the topic of this chapter and are intensively used in engine oils. The overbased detergents are constituted by aggregates of organic salts around a central inorganic core of nanoparticles made of the inorganic base. The organic external shell is therefore able to dissolved in the bulk oil a large amount of the inorganic base, otherwise completely insoluble in the lubricant (*Figura 57*). The organic portion of the detergent, called *soap*, has therefore the ability to associate with the salts

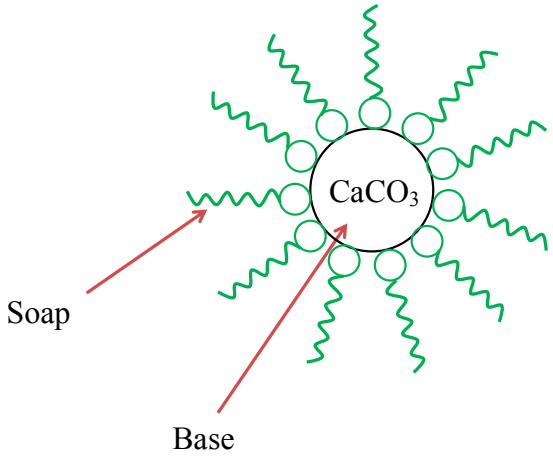


Figure 57 – Structure of a detergent.

to keep them suspended in the lubricant. In a soap it is possible to distinguish two different regions: an active polar functionality, that interacts with the metal salt, and an oleophilic hydrocarbon group with a proper number of carbon atoms to ensure good oil solubility. Sulfonic acids, phenols and carboxylic acids are the common organic acids used in detergent molecules. The most commonly used alkaline earth metal ions are calcium and magnesium ions, generally in the form of carbonate.

The most popular detergents are calcium sulfonates, however, in the last years there is an increasing interest of the petroleum-oil industries in the implementation of sulfur-free detergents, mainly because of environmental issues. In fact, the problem of sulfur content in heavy fuels and oils has been regulated by the European Union since early 2000. The EU have limited the maximum level of sulfur permitted in fuels also in the shipping sector. In fact, heavy fuels and oils used in international shipping, contains 2700 times more sulfur than road fuel/oil. Sulfur contained in fuels and oils, in fact, causes emissions of sulfur dioxide (SO_2) which is oxidises to sulfur trioxide (SO_3) in the atmosphere. The latest gas combining with water present in the atmosphere produces sulfuric acid, an air pollutant responsible of the phenomena of acid rains. Furthermore, sulfur is also connected to the formation of Particulate Matter (PM), the most harmful by-product of diesel engines. Sulfur dioxide in the atmosphere reacts with others pollutants, like nitrogen oxides, and generates a mixture of solid particles called Particulate Matter. This particles have different sizes and shapes and when their diameter is smaller than 10 micrometers (PM_{10}) they are very dangerous for human health because they can be inhaled thus leading to serious

health problems. The reasons explained above are strongly pushing the demand of new sulfur-free lubricants and additives.

4.2 Aims of Research

Due to their ability to form complexes with alkali and alkaline earth metal ions, and to their amphiphilic structure, calixarenes have been proposed as novel sulfur-free surfactants for the synthesis of overbased detergents.[1,2] However, calixarenes must be provide of long branched alkyl groups at the upper rim to ensure oil solubility. In literature, research on the calixarene syntheses have been limited to a few para-alkylphenol precursors such as *p*-*tert*-butyl,[3,4] *p*-*tert*-octyl,[5] *p*-benzyl[6] and *p*-benzyloxy[7] phenols; no studies were found in the literature on the synthesis of calixarenes with branched alkyl groups longer than C_8. Moreover, all the calixarenes known so far, not only are solid at room temperature, but also possess very high melting points and rather low solubilities in organic solvents due to the extensive formation of intermolecular hydrogen bonds between the hydroxyl groups at the lower rim. This low solubility is indeed a positive aspect since it allows the isolation of the macrocyclic compounds from linear oligomers generated in the macrocyclisation reaction and of the calixarenes having different size each from the other. Even the *p*-*tert*-octylcalixarene is a solid quite insoluble in organic solvents also because of the relatively short and regular chain (*t*-octyl is indeed a 1,1,3,3-tetramethylbutyl).

With all these considerations in mind, we proposed *p*-dodecylphenol as a

good candidate for the synthesis of new lipophilic calixarenes with high probability to have a remarkable high solubility in very apolar solvents and in mineral/synthetic oils. The objectives of this research are to study the reaction of formation of calixarenes from *p*-dodecylphenol and to characterise the components of the final mixture. In fact, the outcome of this reaction is a complex mixture of macrocycles with different size accompanied by some starting phenol and a variable amount of linear oligomers. Moreover, due to the great variability of the chains at the upper rim both in terms of number of carbon atoms and position of the branches, that it will be illustrated in details in the next paragraph, the separation of the different components is extremely time and cost demanding.

The second part of the chapter illustrates the studies about the formation of the novel overbased detergent by using the *p*-dodecylcalix[n]arenes. The resulting novel overbased detergents prepared were also tested in different lubricant formulations to evaluate their ability to prevent the formation of residues in the mineral oil.

4.3 para-Dodecylcalix[n]arenes

p-Dodecylphenol (PDP), in the form of its calcium or magnesium sulfonate, is largely used as an additive for lubricants. West European production of PDP in 1985 was around 20.000 tons.[8]

This product is widely diffused because its synthesis is very cheap from an industrial point of view, and the soap has a very good solubility in mineral oils. The synthesis of PDP is illustrated in *Figure 58*.

Propylene tetramers are used as the alkyl portion of the molecule. When propylene, a readily available by-product of petroleum cracking units, tetramerises a large number of isomers are obtained such as those present in *Figure 58*. This mixture is generally called "Tetrapropylene". No attempts are made to separate these isomers for their use in synthetic detergents, because it is neither feasible nor necessary.

In the second step, these tetramers are combined with phenol via a Friedel-Crafts alkylation at a temperature of 100°C through and supported

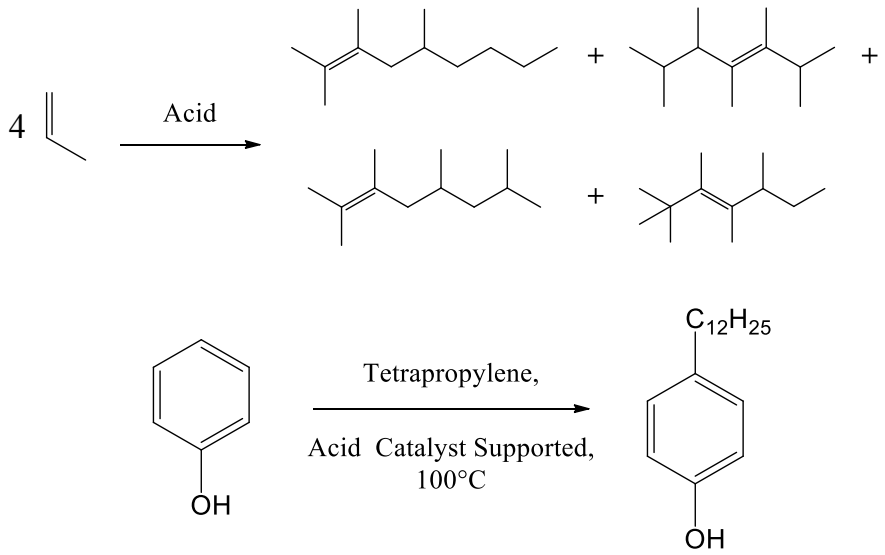


Figure 58 – Synthesis of *p*-dodecylphenol.

acid catalyst. Clearly, again, a number of different isomers are possible and are obtained in these reactions since the phenol group could be linked to any of the secondary or tertiary carbon atoms in the tetramer. This product is therefore far from being a single compound. Again, however, it is not feasible and necessary to separate these isomers, since already the bulk properties of this blend of compounds are appropriate to the application they are devoted for.

Before the study of the synthesis of the *p*-dodecylcalix[n]arenes was started, also with the aim of better characterise this mixture of compounds, PDP was analysed by GC-MS. The result underlined the great variability of PDP in the alkyl chain, and furthermore showed an unexpected outcome.

From the chromatogram, illustrated in *Figure 59*, it is possible to observe

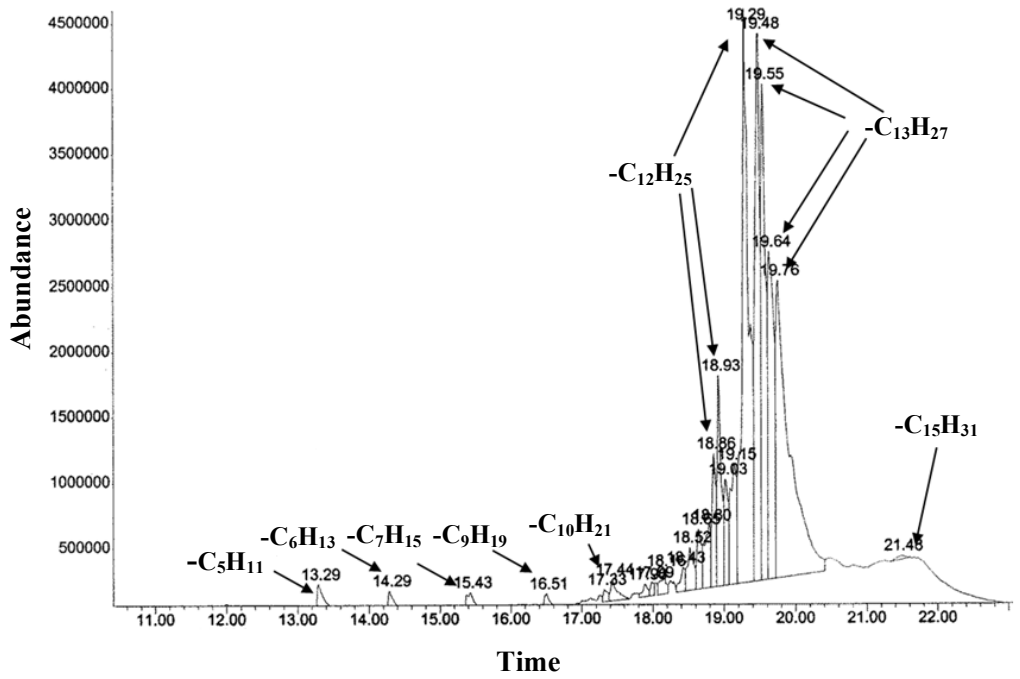


Figure 59 – GC trace of commercial *p*-dodecylphenol.

a really very high number of peaks having very different retention times. For each one of these signals, it was acquired its mass spectrum with the Electron Impact Ionisation, thus allowing to recognise the different type of compounds present in the phenols. *Figure 59* reveals that indeed are present phenols with alkyl chains from five to fifteen carbon atoms, the most abundance ones being phenols with C_{12} and C_{13} alkyl chains. For these last two compounds it was easy to outline the presence of different structural isomers probably having different number and position of the branches in the alkyl chain. The presence of such a large amount of different compounds was quite unexpected and suggests that also the propylene used in the synthesis of PDP is indeed a mixture of different compounds such as, probably, ethylene or butylene.

This high variability in the number of compounds and isomers of PDP will clearly strongly affect the physical and chemical properties of the *p*-dodecylcalix[n]arenes, as it will be shown in the next section. From here on, in all the chemical structure where PDP is involved and in cyclic or linear oligomers, the $-C_{12}H_{25}$ substituent will imply a mixture of all the possible alkyl chains from C_5 to C_{15}, linear or with different number and position of their branches.

4.3.1 One-pot synthesis of p-dodecylcalix[n]arenes

The reaction for the synthesis of *p*-dodecylcalix[n]arenes was studied in details in the last years by this research group especially in order to maximise the conversion of the linear oligomers into calixarenes. Moreover, the conditions have been optimised to increase the conversion

of all the initial PDP. These studies led to a synthesis divided into two steps, carried out in the same reactor.

In the first phase the condensation between *p*-dodecylphenol and formaldehyde in slight excess (1.2 equivalents), through basic catalysis, is taking place. The reaction is carried out at about 120°C and water is removed from the reaction vessel by a Dean-Stark apparatus. During this phase the formation of the linear oligomers having a different number of units is observed, as it can be monitored by TLC and APPI-MS analysis. The second step starts when almost all the theoretical water produced in the first phase is recovered (about two hours).

Then xylene is added to the reaction mixture and the temperature is increased to 140°C for four hours. Thanks to reflux, the last traces of water are removed again by a Dean-Stark apparatus in order to favor the cyclisation of the macromolecules. At the end the reaction mixture is

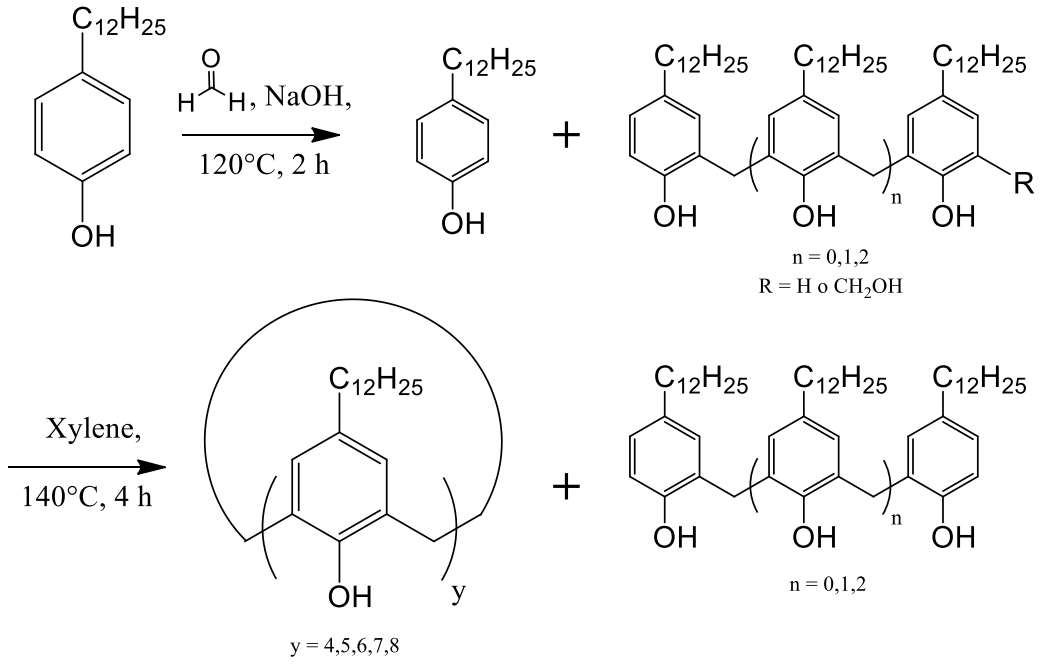


Figure 60 – Synthesis of *p*-dodecylcalix[n]arenes.

concentrated under vacuum until a concentration of 77.5% w/w in xylene is reached. The resulting mixture of phenol condensation products and xylene is a very viscous oil also because of the inhomogeneous chains at the upper rim of the calix[n]arenes prevents the precipitation of the macrocyclic structures even from this highly concentrated solution. The final composition of the phenolic products was established by HPLC analyses carried out in the laboratories of San Donato Milanese. The analysis was achieved using a C_{18} column and an initial eluent of EtOH:H_2O = 95:5. During the analyses the polarity of the eluent was increased to EtOH:H_2O = 90:10. The final composition was established to be about 80% of calixarenes, 16% of oligomers and 4% of unreacted PDP. The main components in the crude product were determined by APPI-MS in a negative ionisation mode. The great advantage of the APPI-MS

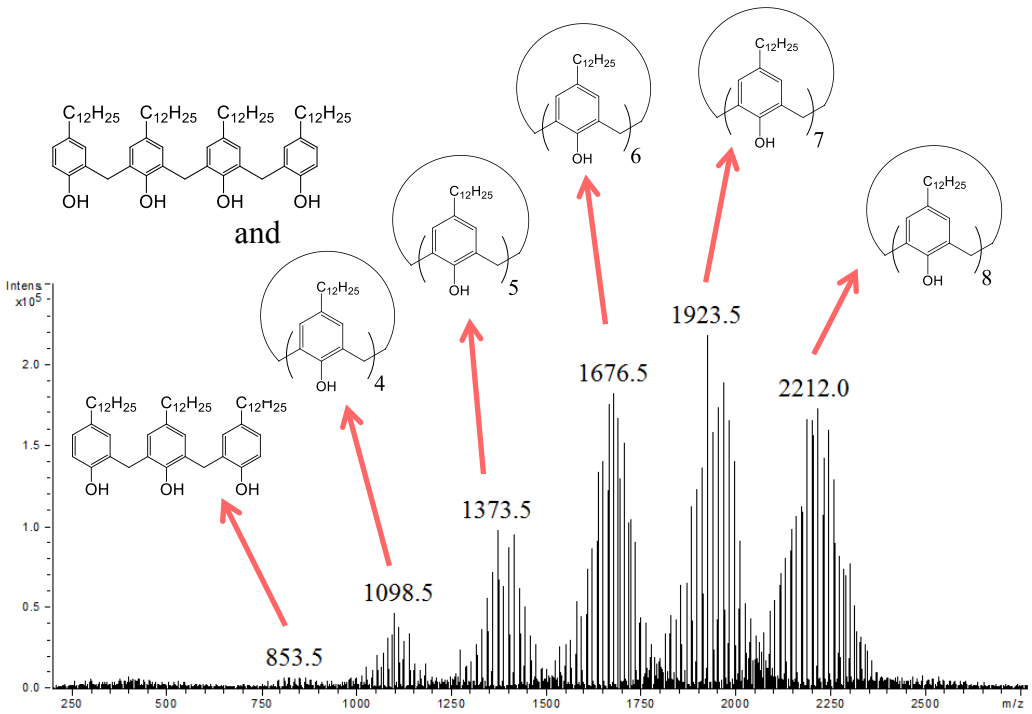


Figure 61 – APPI-MS spectrum of the *p*-dodecylcalix[n]arenes mixture.

analysis is that it prevents the problem of low solubility of the sample since it uses toluene as solvent. In fact, with ESI-MS, it is not possible to acquire any spectrum due to the very low solubility of the *p*-dodecylcalix[n]arenes in MeOH or ACN/acetone, the most common solvents used with such technique. *Figure 61* shows a typical distributions of peaks in the MS spectra originated by this kind of products and caused by the great variability of the alkyl chains at the upper rim of the macrocycles. What can be clearly seen in this spectrum is the large abundance of the cyclic compounds with a number of aryl units equals to 4, 5, 6, 7 and 8 over a small presence of linear oligomers with three and four units.

To confirm the successful outcome of the reaction it was also recorded a ^{1}H NMR spectrum of the crude product. The spectrum in *Figure 62* is characterised by very broad signals caused by the inhomogeneous chains of the macrocycles and by the conformational mobility of calixarenes that are characterised by life-times comparable to time scale of the technique. However, the spectrum shows four main areas. At high fields are present the signals of the alkyl chains at the upper rim which, again, are rather broad due to the wide variability of these chains. Then moving towards low fields it is possible to localise the signals of the hydrogens of the methylene bridge. In this area it is possible to observe the overlap of the different signals belonging to calixarenes having different sizes. Quite interestingly, it is also possible to note the absence of sharp singlets around 3.9 ppm or between 4.6-4.8 ppm due to the $ArCH_2Ar$ and CH_2OH units, respectively, of conformationally mobile linear oligomers. At 7.09 ppm is present the singlet of the aromatic hydrogens of

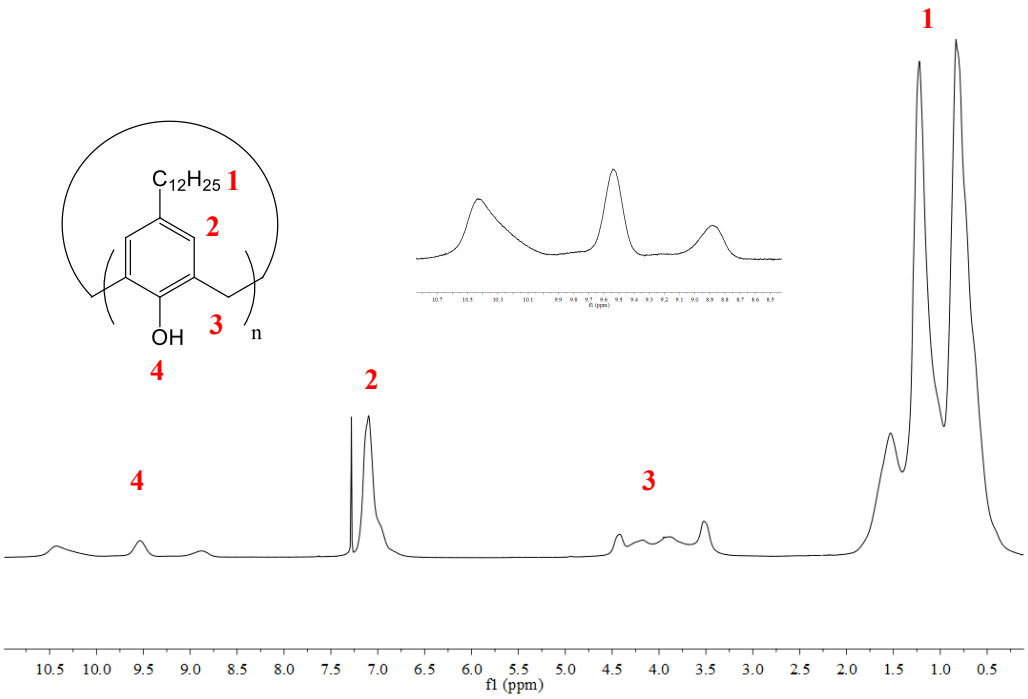


Figure 62 – ^{1}H NMR spectrum of *p*-dodecycalix[n]arenes (300 MHz, $CDCl_3$, 25°C).

the calixarenes, and at very low fields, due to the intramolecular hydrogen-bonds that strongly deshield these protons, are located the broad signals of the hydroxyl groups. This effect can be considered another proof of the extremely high occurrence of cyclisation products, since linear oligomers would give rise to a wide series of multiplets for the aromatic protons around 7 ppm and sharp singlets for the OH group located between 5.5 and 6.5 ppm.

However, the expansion in the offset of *Figure 62* reveals that the overlapping of the OH signals is not so large like for the peaks of the methylene bridges. In fact, it is possible to recognise three main broad signals that fall at 10.44 ppm, 9.53 ppm and 8.89 ppm. Moreover, under the peak at 10.44 ppm it seems to be presented at least another broad signal. It can be thus suggested that at least four macrocycles differing in

size are the most abundant species in the mixture, while the other ones detected by APPI-MS are present in much lower percentage. The next paragraph will describe the separation of the main components of the mixture.

4.3.2 Separation and characterisation of the main components

The inhomogeneous chains at the upper rim of the calix[n]arenes makes impossible the separation of the macrocycles differing for the size by precipitation or crystallisation. So, in order to have a more detailed characterisation of the mixture of products, it was made an attempt to separate the different compounds by chromatography.

First of all, the linear oligomers were separated from the mixture of products to facilitate the purification of the macrocycles. It was discovered that the linear oligomers, and the PDP, are rather more soluble in methanol than the *p*-dodecylcalix[n]arenes. The crude mixture of products was therefore stirred in methanol at room temperature for 24 hours and, afterwards, an orange solid was isolated by filtration, while the solvent was evaporated to dryness from the filtrate to give an orange oil. *Figure 63* shows the APPI-MS spectrum recorded in negative ionisation mode for the oil obtained from the methanol which, as expected, was mainly composed by unreacted PDP and linear oligomers.

Then the orange precipitate was analysed by TLC. Using a low polarity mixture of eluents, it was observed that the precipitate was composed by a series of spots with high intensity and a high R_F and by small spots with

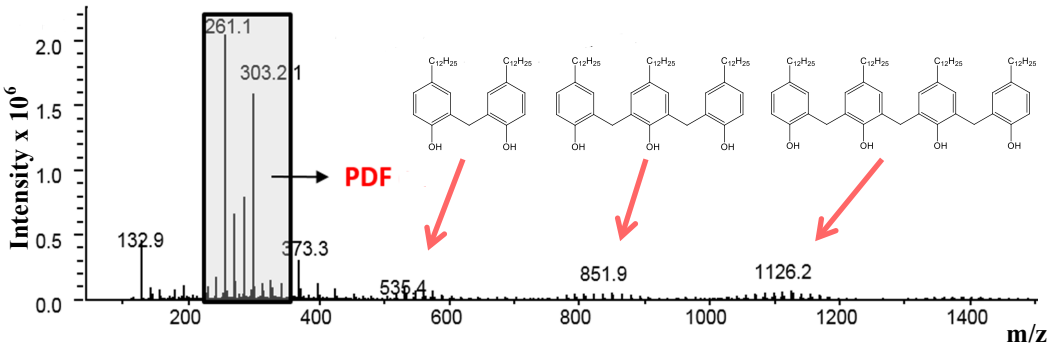


Figure 63 – APPI-MS spectrum of the mother liquids.

low R_F. The first series of spots was assigned to the macrocycles, while the other ones to the linear compounds that partly coprecipitated from the crude mixture.

In order to reach the final goal of the isolation of the different macrocycles, a flash chromatography separation was carried, starting with a very apolar eluent such as hexane : diethyl ether = 99:1. Subsequently the polarity of the eluent was gradually and carefully increased (hexane : diethyl ether = 96:4) to favor the elution of the more polar compounds until all the mixture was eluted. After the separation, the different fractions were analysed by NMR spectroscopy. The obtained spectra clearly pointed out that the fractions were considerably less complex compared to the initial mixture but also suggested that the flash chromatography column alone was not sufficient to completely separate the pure compounds. So, the single fractions were further purified by preparative TLC and new fractions were produces. The preparative TLC plates were charged with rather small quantities, between 10 and 20 mg, of compounds from the flash chromatography separation to have a favorable calixarene/silica gel ratio which favor the macrocycle

separation. Using hexane : diethyl ether = 99:1 as eluent, the main components were therefore separated and characterised in this way.

The faster product (**29**) results to be the most abundant of the mixture of macrocycles, and its ^{1}H NMR spectrum allows to point out that it gives rise to the broad signal at 9.53 ppm (*Figure 64*, next page). Moreover, always from the spectrum it is possible to note that **29** is a calixarene: the two protons of the methylene bridge give rise to two separate peaks suggesting that the conformational interconversion is somehow slowed down on the NMR time-scale, due to the formation of strong intramolecular hydrogen bonds among the -OH groups at the lower rim.

In order to establish the size of the cycle it was necessary to resort to the MALDI-TOF instrument because, as already said, these compounds are not soluble in the solvents used by the ESI-MS.

From the analysis of the spectrum in *Figure 65* (next page), it can be stated that **29** is a calixarene with eight aryl units. Interestingly, the distribution of molecular masses is centered on the value of 2230 m/z that can be interpreted as a calix[8]arene with seven C_{12} alkyl chains and one C_{13} residue. Due to the peculiar composition of *p*-dodecylphenol, already explained, all the mass spectra of these calixarenes are characterised by a wide distribution of peaks. Each of these cluster of peaks is centered around more prominent signals corresponding to a calixarene with all the alkyl chains having 12 C atoms or with one alkyl chain having 13 C atoms and the remaining chains of 12 C atoms. On the left or on the right of these statistically more favored compounds it is always possible to observe other peaks spanned by 14 uma which correspond to calixarenes differing from the number of CH_2 moieties compared to the previous ones.

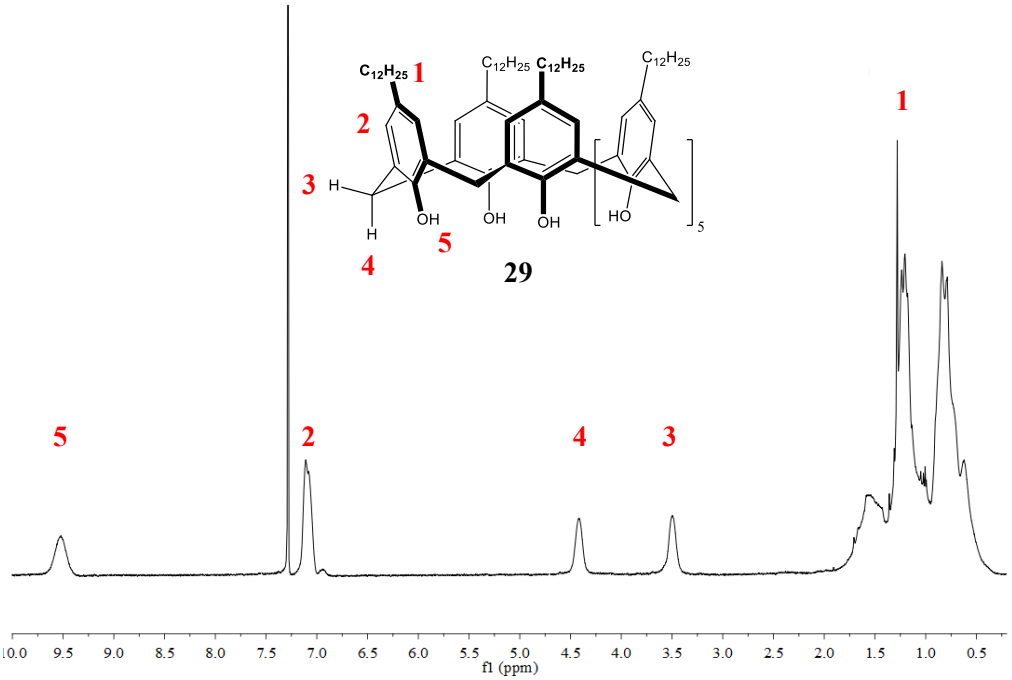


Figure 64 – ^{1}H NMR spectrum of **29** (400 MHz, $CDCl_3$, 25°C).

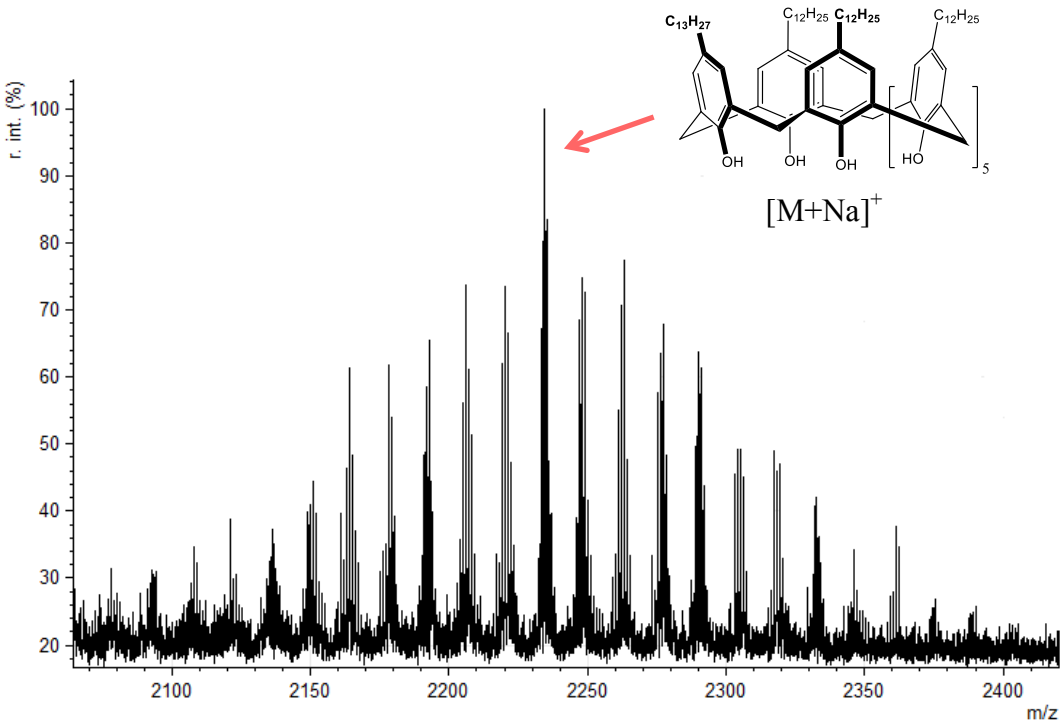


Figure 65 – MALDI-TOF spectrum of **29**.

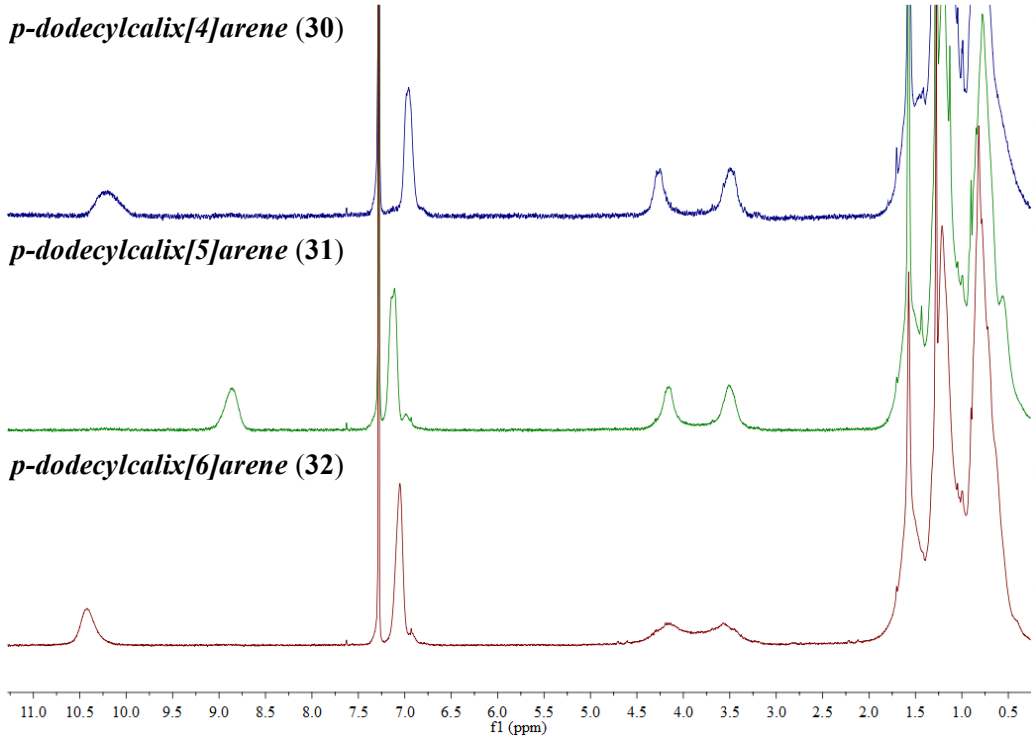


Figure 66 – From the top to the bottom: ^{1}H NMR spectrum of **30** (400 MHz, $CDCl_3$, 25°C), ^{1}H NMR spectrum of **31** (400 MHz, $CDCl_3$, 25°C) and ^{1}H NMR spectrum of **32** (400 MHz, $CDCl_3$, 25°C).

Continuing with the preparative silica plate separation it was possible to isolate other compounds, that, again thanks to the MALDI-TOF spectroscopy, were determined to be macrocycles differing in their size. In *Figure 66* are reported the ^{1}H NMR spectra of other three macrocycles of the mixture **30**, **31** e **32** that were respectively assigned to be the *p*-dodecylcalix[4]-, the *p*-dodecylcalix[5]- and the *p*-dodecylcalix[6]arene. The order of elution was: calix[4]-, calix[6]- and calix[5]arene.

What is interesting to note is the difference in ppm of the signal of the hydroxyl group for these three compounds: for the calix[4]- and -[6]arene the peak fall respectively at 10.22 ppm and 10.44 ppm while the peak of

the calix[5]arene is located at 8.86 ppm. In general, therefore, it seems that the hydrogen bonds at the lower rim of the calix[n]arenes are stronger in the calix[4]- and in the calix[6]arene leading to peaks at lower fields compared to the calix[5]arene. However, although the hydrogen bonds are stronger in the calix[6], the shape of the two peaks of the methylene bridge seems to indicate that the calix[6]arene is more mobile and closer to the coalescence temperature.

Furthermore, it was also possible to isolate another compound (slower respect to the others in the elution) with an ^{1}H NMR spectrum similar to those of the previous compounds and that should be cyclic. The spectrum of **33** is reported in *Figure 67* and shows that the product seems to be another calix[n]arenes. In fact all the signals of the calixarene platform are present and moreover the peaks of the methylene bridge are affected by

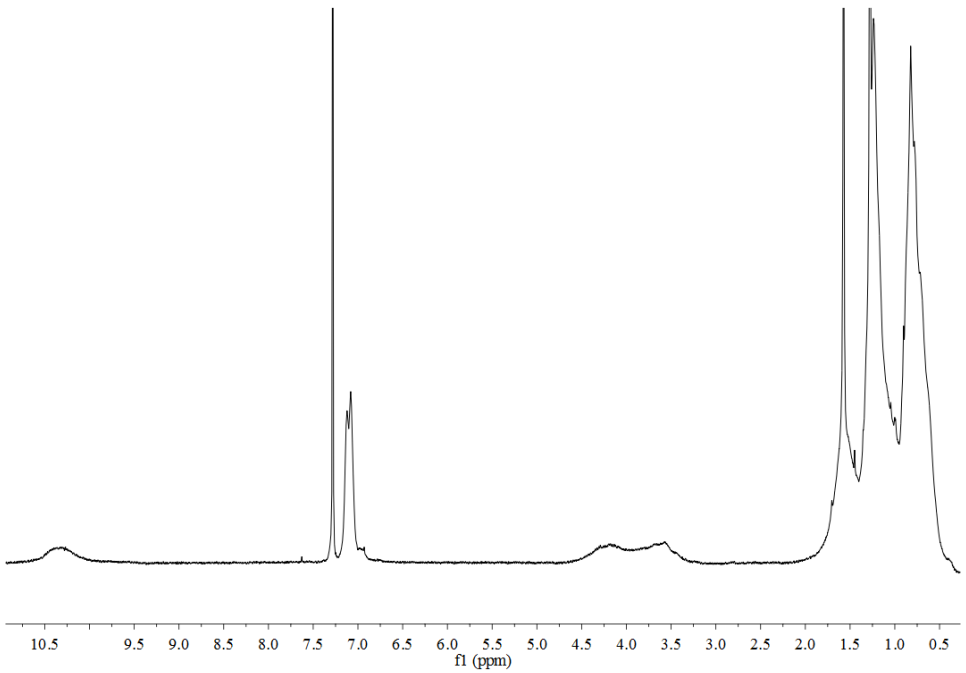


Figure 67 – ^{1}H NMR spectrum of **33** (400 MHz, $CDCl_3$, 25°C).

the same phenomena of the *p*-dodecylcalix[6]arene.

Unfortunately, it was not possible to establish the size of **33**, because the sample did not ionise under the same experimental conditions used also for the other compounds in the MALDI-TOF. However, considering the APPI-MS spectrum of the mixture (*Figure 61*) and that calix[4]-, -[5]-, -[6]- and -[8]arene were already previously isolated, the structure of compound **33** should be assigned to the *p*-dodecylcalix[7]arene.

Taking into consideration the quantities of all the purified macrocycles, it was determined a general composition of the calixarenes in the mixture. The most abundant product is the *p*-dodecylcalix[8]arene with a percentage of 33.0%, followed by the *p*-dodecylcalix[5]arene (26.3%) and the *p*-dodecylcalix[6]arene (21.4%). Compound **33**, the hypothetical *p*-dodecylcalix[7]arene, is approximately 14.8% while the *p*-dodecylcalix[4]arene is present in a rather small amount equal to 4.5%.

To confirm that the main components of the mixture of calixarenes were isolated, the ^{1}H NMR spectra of all the purified macrocycles were superimposed and the result was compared it with the spectrum of the mixture. *Figure 68* shows the part of the spectrum between 8.5 and

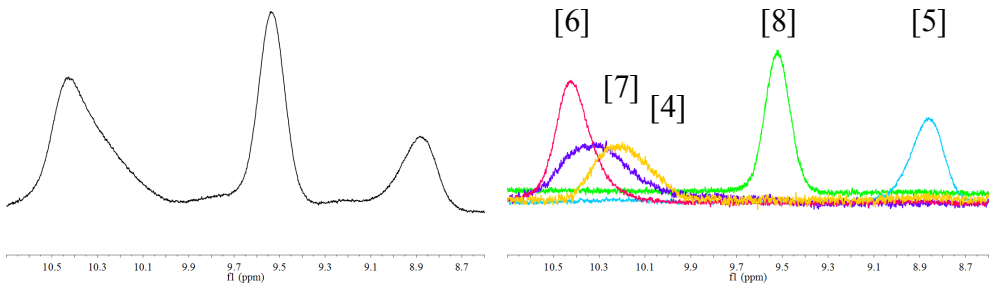


Figure 68 – Comparison between the OH group portion of ^{1}H NMR spectrum of the mixture and the overlapping of the spectra of the purified compounds.

11.0 ppm. What can be clearly seen is that the principal peaks of OH groups in the mixture belongs to the OH group of the isolated *p*-dodecylcalix[n]arenes.

It is also interesting to note that all the spectra of the purified macrocycles show, for the hydrogens of the methylene bridge, two broad signals. For a calixarene in the cone conformation, the two hydrogens of the bridge are not chemically equivalent and give rise to two well separated doublets characterised by a geminal coupling constant (14-15 Hz). The doublet at low fields belongs to the hydrogen in axial position while the doublet at high fields belongs to the hydrogen in equatorial position. However, from the recorded spectra of *p*-docedylcalix[n]arenes, a quite different picture can be evidenced.

Already at room temperature and regardless of the size, the ^{1}H NMR spectra of these macrocycles shows two distinct signals at the typical chemical shift values of axial and equatorial protons of cone conformation, but these signals lack of the typical geminal constants. To shed light on this anomaly, a series of spectra at low temperatures of the *p*-dodecylcalix[8]arene were recorded, to verify if the decrease of the kinetic rate of conformational interconversion would have led to definition of the two doublets. *Figure 69* reveals that also at -30°C the situation remains fundamentally unchanged. This suggests that the signal of the two hydrogens of the bridge are not appearing as doublets because affected by a great variability of the branched alkyl chains at the upper rim of the calixarenes. The two signal thus generated can therefore be explained as the superimposition of several doublets slightly differing in their chemical shift values and for this reason generating broad signals.

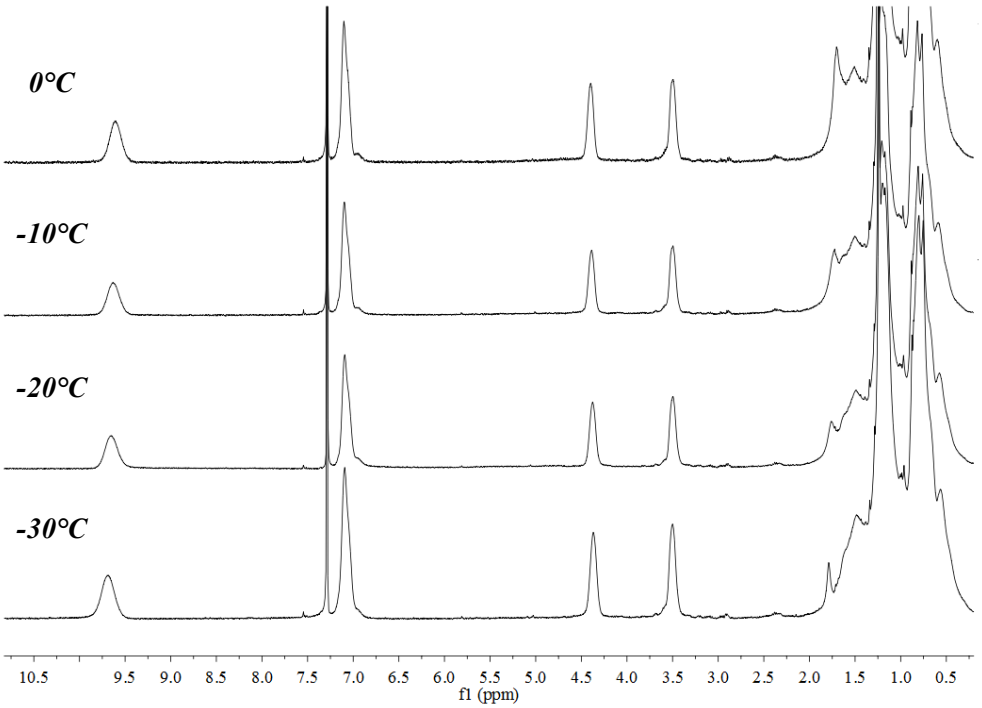


Figure 69 – ^{1}H NMR spectra ($CDCl_3$, 400 MHz) at low temperatures of *p*-dodecylcalix[8]arene (**29**).

However, spectra at high temperatures were recorded to observe the coalescence of the signals of the methylene bridge, as already done for the simple *p-tert*-butylcalix[8]arene by *Gutsche et al.*[9]

Figure 70 shows the enlargement in the central area of the spectra recorded at room temperature and at high temperatures in 1,1,2,2-Tetrachloroethane-d_2. It was necessary to use this solvent because **29** is not soluble in DMSO and moreover the coalescence temperature was higher respect to the boiling point of chloroform.

What can be clearly seen from the picture is that the temperature of coalescence is at 70°C. Considering the equation of Eyring, the free energy of activation for the conformational inversion of **29** was calculated

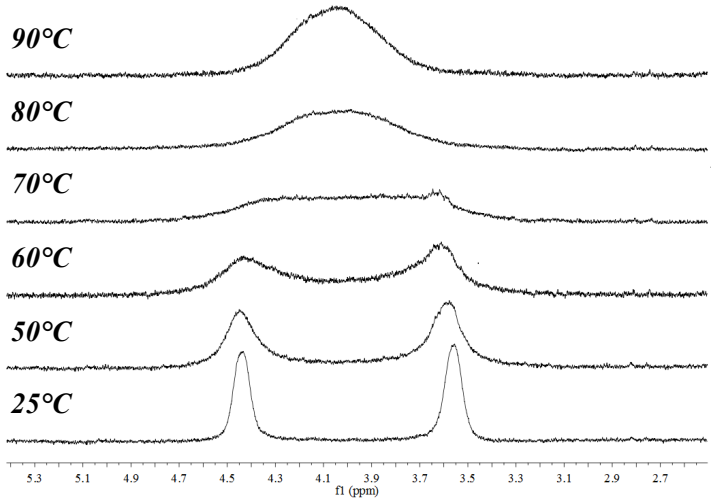


Figure 70 – ^{1}H NMR spectra ($CDCl_2CDCl_2$, 400 MHz) at high temperatures of *p*-dodecylcalix[8]arene (**29**).

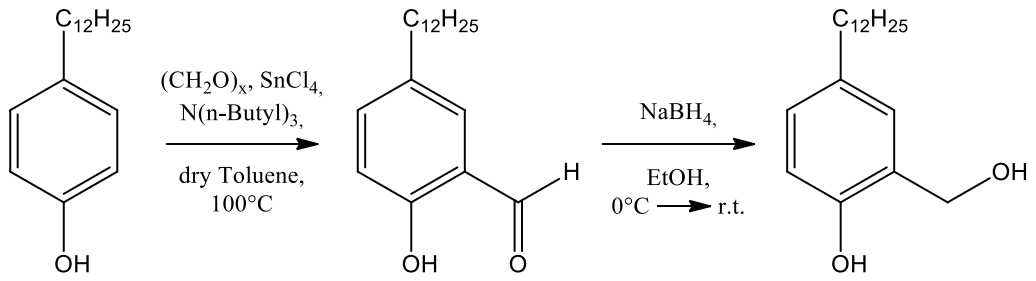
in 14.9 kcal/mol. *Gutsche and coworkers* reported a value of 15.7 kcal/mol for the simpler *p-tert*-butylcalix[8]arene.[9] Contrary to what expected, *p*-dodecylcalix[8]arene that bears larger alkyl substituents, has therefore an interconversion energy barrier value slightly lower respect to that of *p-tert*-butylcalix[8]arene. It should however be remembered that our calculation is made in a different solvent (deuterotetrachloroethane) respect to the experiment of *Gutsche et al.* (deuterochloroform). The difference in energy is however not that different and, in any case, suggests that, as widely reported in the literature,[10] when bulky groups are present in para position the conformational interconversion takes place via a mechanism called oxygen-through-the-annulus. This obviously implies that the difference in energy is not too different in the two cases and it's probably affected more by solvation effects or by cavity-included solvent molecules than by the structurally different substituents at the upper rim.

Finally, we also tried to characterise the mixture of the last compounds eluted from the column, attributable to linear oligomers. These compounds are present in low quantities in the mixture, probably less than 5%, give rise to the rather complicated NMR spectra and give no significant peaks neither in MALDI-TOF nor ESI-MS spectra. It is possible to hypothesise that these species are linear oligomers, maybe in mixture with oxa-calixarenes formed during the reaction.

4.3.3 Synthesis of linear oligomers

The complete characterisation of the mixture is important to understand which are the species that are formed during the reaction. On one side this will help in trying to push further the reaction in order to increase the yield of macrocycles, on the other side, it will be useful to understand the degree of oligomerisation of the linear compounds since also the latter oligomers may play a role in detergent preparation.

On this line, it was decided to synthesise some of the shorter linear oligomers that, as standard, would have helped in the definition and characterisation of the linear components of the reaction mixture originated during the preparation of the *p*-dodecylcalix[n]arenes. The syntheses were focused firstly on the monomeric and dimeric linear oligomers terminating with a -H or with a $-CH_2OH$ groups. The APPI-MS analysis never showed the presence of linear oligomers terminating with $-CH_2OH$, however they have been isolated in the synthesis of calixarenes with other groups in para position such as *tert*-butyl. So it was decided to synthesise also this kind of linear products.



34 **35**

Figure 71 –Synthesis of compound **35**.

The first compound to be obtained was compound **35**. In *Figure 71*, the synthetic pathway proposed for this compound is shown. In the first step it was synthesised the corresponding salicylaldehyde derivative (**34**). The reaction was carried out with formaldehyde and a catalytic amount of tin (IV) chloride in the presence of tributylamine to neutralise the hydrochloric acid produced during the reaction.[11] The final product was separated by the unreacted PDP by flash chromatography and obtained in a yield of about 20%. Its structure was confirmed by NMR spectroscopy and ESI-MS. In the following step, product **34** was reduced to **35**, using sodium borohydride in ethanol, following the classical conditions.[12]

In *Figure 72*, it is reported the ^{1}H NMR spectrum of derivative **35**. What stands out is the influence of the inhomogeneous chain in para position on the signal shape of the spectrum. In particular, the aromatic hydrogens in position 2 and 3 are affected in a larger way by the variability of the chain, in fact their signals are rather complex, as illustrated in the enlargement. Instead the peaks of the hydrogens in position 4 and 5 give rise to simpler signals since they are distant from the alkyl chain.

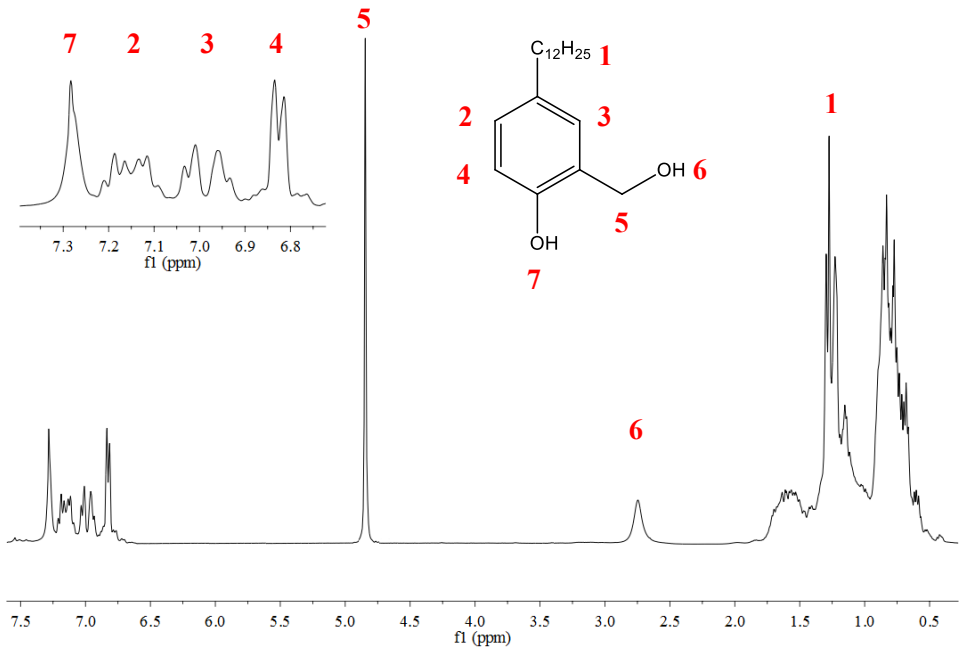


Figure 72 – ^{1}H NMR spectrum of **35** (400 MHz, $CDCl_3$, 25°C).

Moreover, the broad signal of the benzyl hydroxy group (marked as number 6) resonates at 2.75 ppm, while the hydroxy group of the phenol is located at about 7.26 ppm, partially superimposed with the peak of the residual $CHCl_3$.

Derivatives **36** and **37** were obtained from a single reaction. In literature it was reported that the reaction between *tert*-butylphenol and formaldehyde in presence of a base such as sodium hydroxide, potassium hydroxide or potassium carbonate, at about 40°C leads to the formation of the *tert*-butyl

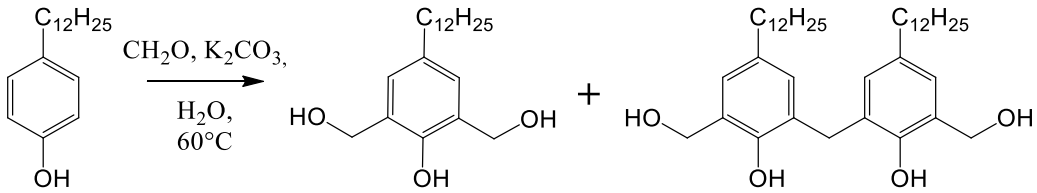


Figure 73 – Synthesis of derivatives **36** and **37**.

analogs of **36** and **37**.[13–16] Moreover, increasing or decreasing the time of reaction is possible to obtain only the linear monomer **36** or both derivatives **36** and **37** in a different yields.

After many attempts in which different combinations of bases and reaction times were tested, the best result for the *p*-dodecylphenol in terms of yield was obtained using potassium carbonate and three days of reaction at 40°C. The final mixture included different compounds, together with compounds **36** and **37** it was observed by TLC analysis also the presence of the monohydroxymethylated compound **35**, although in a sharply lower concentration. It was therefore necessary a chromatographic separation to purify the desired products.

The ^{1}H NMR spectrum of derivative **36** was in accord to the expected spectrum, and further confirmation of its identity came from the ESI-MS spectrum where a peak at a value of 345.5 m/z and belonging to the $[M+Na]^{+}$ adduct of the product was observed.

Some discrepancies were, on the other side, found in the ^{1}H NMR spectrum of compound **37**. Although the signals of the different hydrogens resonate at the expected values of chemical shift, their integrations are consistently different from the expected ones. To ascertain the identity of this product, was therefore necessary to acquire an ESI-MS spectrum (*Figure 74*). As expected, also in this case the spectrum is characterised by the typical distribution of signals originating from the inhomogeneity of the alkyl chains of the starting *p*-dodecylphenol. Unexpectedly, the spectrum is characterised by two main distributions: the highest one is centered at m/z = 649.7, while the second one is at m/z = 1276.5. Since the molecular mass of **37** is equal to

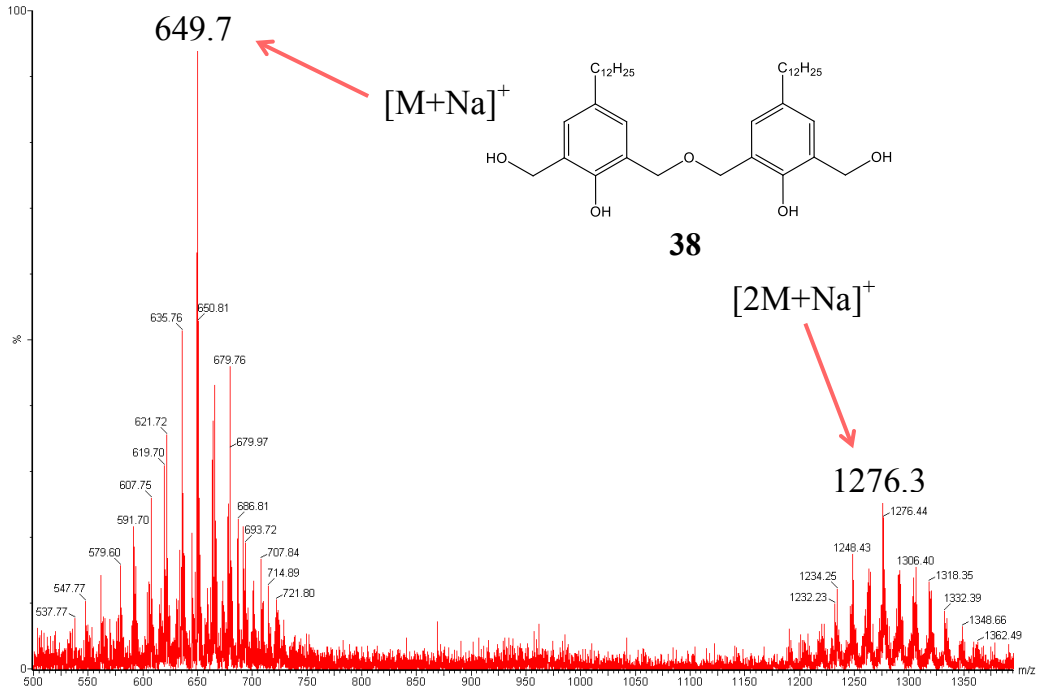


Figure 74 – ESI-MS spectrum of **38**.

596 amu, a possible adduct with sodium should be found at m/z = 619. These distributions are therefore quite faraway (30 amu lower) from this value and clearly suggested that did not belong to the dimer **37**. However, after some different hypothesis it was understood that an additional -CH_2O- group was present.

The ESI-MS spectrum belongs therefore to derivative **38**, a dimer very similar to **37** but with an ether linkage in the middle. This outcome was surprising, from one side, because in literature there are no data about the formation of a similar product under these conditions but, from the other side could be expected since these bridged are well known to form as intermediates of oxacalixarenes. Coming back to the ESI-MS spectrum, the base peak of the first distribution is due to compound **38** with two chains of twelve carbon atoms, while the highest peak of the second

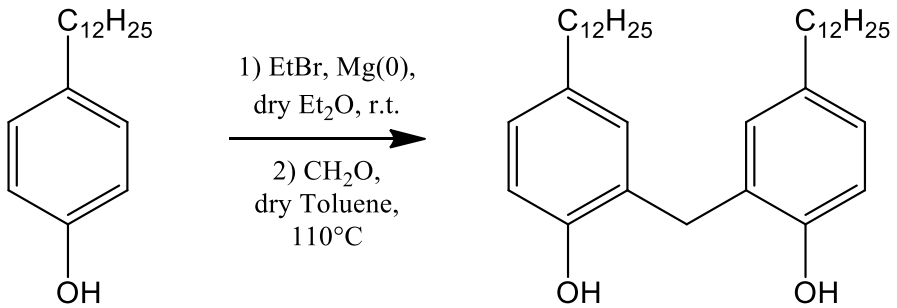
distribution is an adduct between two molecules of the dimer plus a sodium ion, as frequently observed in the ESI-MS spectra of these class of polyphenols.

Moreover, after further insights with ^{13}C NMR and HSQC spectra, it was concluded that the fraction isolated from the column, not only contained, as the main compound **38** but also some amounts of compounds **36** and **37** are present. However compounds **38**, although not completely pure, was used as standard for the characterisation of the mixture deriving from reaction of preparation of calixarenes.

So far this paragraph has focused on the synthesis of linear oligomers with ending CH_2OH groups. In the following part the synthesis of linear oligomers ending with hydrogen atoms will be discussed.

Dimer **39** was prepared by adapting the procedure used by *Casiraghi et al.*[17] on the *tert*-butylphenol. The acylation reaction with formaldehyde was in this case carried out starting from *p*-dodecylphenoxymagnesium bromide since magnesium is a superior Lewis acid catalyst for the ortho-selective functionalisation of phenols with aldehydes in aprotic polar media.

The first step of the reaction led to the formation in situ of the



39

Figure 75 – Synthesis of derivative **39**.

p-dodecylphenoxymagnesium bromide. In the second phase, toluene and paraformaldehyde, in a slight defect, were added and the mixture was mixed and heated at 110°C for 18 hours. The amount of paraformaldehyde is crucial since with larger contents the reaction continues generating longer oligomers.

After quenching the desired product was purified by flash chromatography. The fraction hypothesised to contain compound **39** was submitted to mass spectrometry that pointed out that it was composed by a mixture of dimer (**39**) and trimer (**40**). *Figure 76* shows the ESI-MS spectrum of the column fraction acquired in negative ions. The smaller distribution on the left belongs to the desired product **39** while the higher peaks of the distribution on the right originates from the trimer **40**. Other

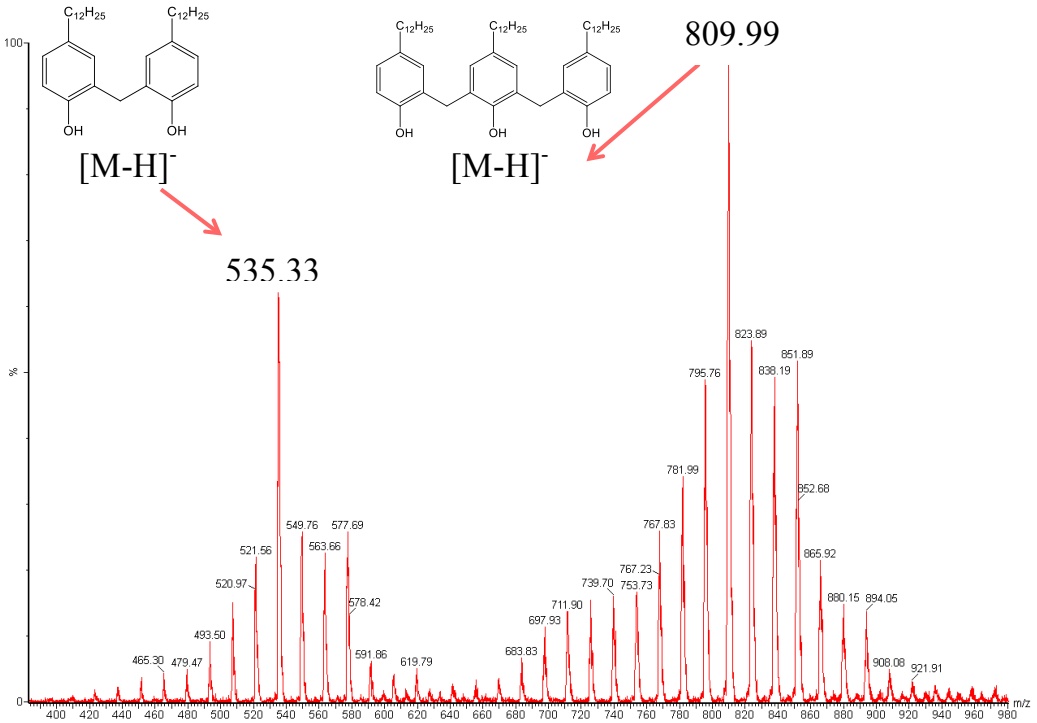
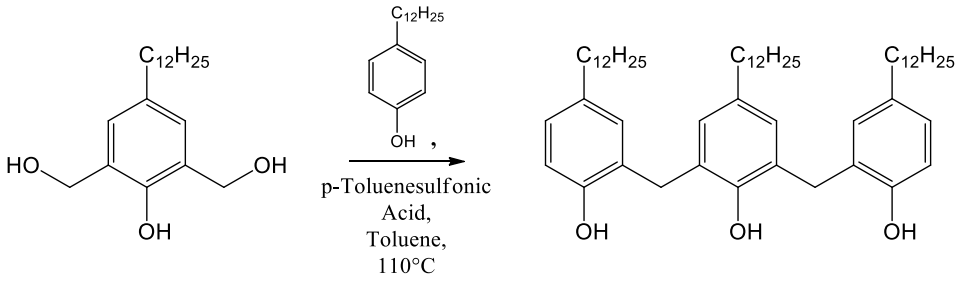


Figure 76 – ESI-MS spectrum of the column fraction containing compounds **39** and **40**.



36 **40**

Figure 77 – Synthesis of derivative **40**.

attempts to separate through column chromatography the mixture of these two compounds, unfortunately, failed resulting thus impossible to obtain pure samples.

It was then decided to synthesise the trimer **40** through the reaction in *Figure 77* in order to have access at least to a pure single linear oligomer terminating with hydrogen atoms. In literature it was reported the synthesis of a similar trimer starting from 2,6-bis-hydroxymethyl-4-*tert*-butylphenol (analogous to **36**) with an excess of *p*-cresol catalysed by *p*-toluenesulfonic acid.[18] Therefore the reaction was repeated using compound **36** and *p*-dodecylphenol as reagents. At the end compound **40** was purified by flash chromatography to remove the excess of *p*-dodecylphenol. The NMR spectroscopy and the mass spectrometry confirmed the formation of the trimer and, moreover, the ESI-MS spectrum showed the same distribution centered on the value 809.99 as found in the spectrum (see *Figure 76*) of the mixture of compounds **39** and **40**.

At this point the linear oligomers **35**, **36**, **38** and **40** were characterised completely by ^{1}H NMR and ^{13}C NMR spectra, and the results were compared with the spectra of the final reaction mixture for the preparation

of *p*-dodecylcalix[n]arenes in order to eventually verify the presence of these compounds.

The ^{1}H NMR spectra of **35** and **40** in *Figure 78* (bottom and middle traces, respectively) show at 6.83 ppm the signal of the H atoms in ortho to the phenolic hydroxyl group. For compound **35** it is possible to observe the doublet due to the coupling with its ortho aromatic hydrogen, while for **40** the peak is broader probably because it is more deeply affected by the great variability in para position of the chains. Considering the reaction mixture, the macrocycles cannot give rise to signals at this values

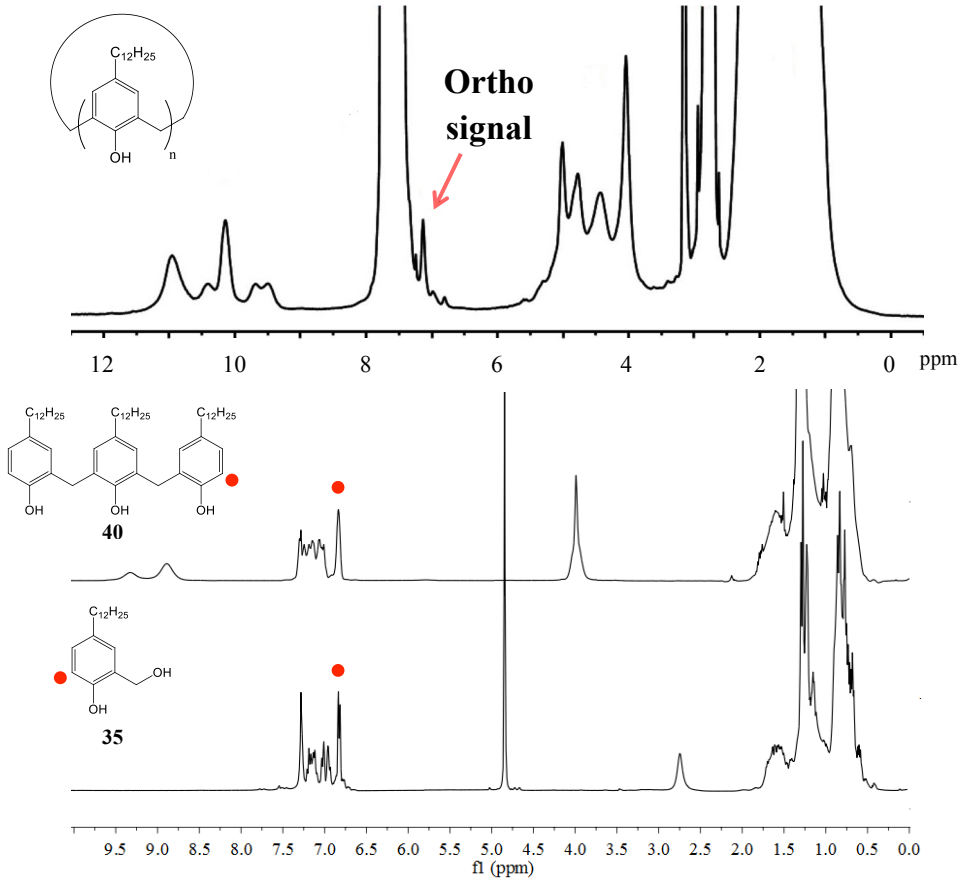


Figure 78 – Comparison between ^{1}H NMR spectra of the reaction mixture for the preparation of *p*-dodecylcalix[n]arenes (top), **40** (middle) and **35** (bottom).

of chemical shifts since the ortho position to the hydroxyl group is occupied by the methylene bridge groups. However, observing the ^{1}H NMR spectrum of the final mixture at 7.10 ppm is located a little broad signal. This peak could only be generated by linear oligomers of type **35, 40** or higher mass proving therefore their presence in the mixture. It should be said that, potentially, also unreacted PDP could generate this signal but after a ^{1}H NMR analysis of the *p*-dodecylphenol it was inderred that its "ortho" doublet resonates at a little bit lower ppm value, and exactly at 6.75 ppm. In conclusion this result is another proof of the presence of linear oligomers or ortho-species in the mixture.

Moreover, it is also quite interesting to note that the broad signals of the phenolic OH groups of **40** fall between 9.50 ppm and 8.75 ppm, so it is reasonable to believe that under the signals of the hydroxyl groups of the reaction mixture are hidden also the signals of the linear oligomers.

Another significant aspect was revealed comparing the ^{13}C NMR spectrum of the reaction mixture with that of **38**. *Figure 79* reveals in the spectrum of the reaction mixture of a little peak at about 70 ppm. This is unusual for the classical signals of the calix[n]arenes which show the $ArCH_2Ar$ carbon bridge at 30-32 ppm and also for the linear oligomers where the analog signals are also located around 32 ppm. Carefully observing the spectrum of dimer **38**, the peak of the carbons in the CH_2OCH_2 group resonates at 70.6 ppm that is very similar to that one detected in the spectrum on the reaction mixture (top). This finding broadly supports the idea that in final mixture are present, in very few concentrations, also species with ether linkages such as linear compounds **38** or oxa-calixarenes.

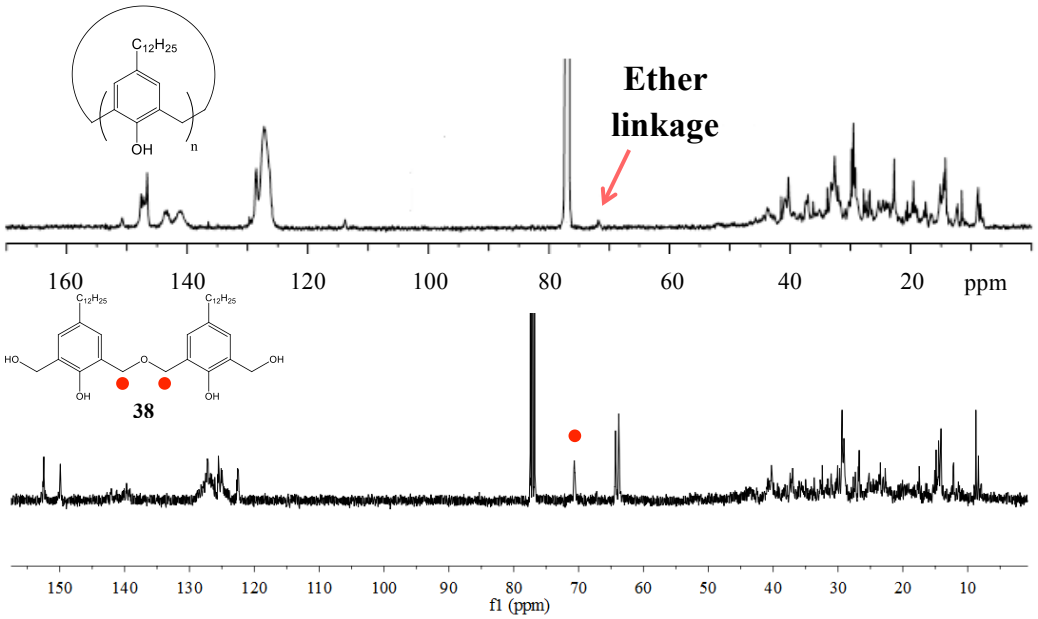


Figure 79 – Comparison between ^{13}C NMR spectra of the reaction mixture of the synthesis of *p*-dodecylcalix[n]arenes (top) and **38** (bottom).

In addition to this, in the ^{13}C NMR spectrum of the reaction mixture there is another little peak at about 115 ppm, unexpected for the calixarenes series. This signal is due to the aromatic carbon in ortho position respect to the hydroxyl group in the linear oligomers terminating with an hydrogen atom (such as **39** or **40**). This is an interesting observation since suggests that linear oligomers having terminal hydrogen atoms are present and probably they do not further or completely react to the yield calixarenes because of the complete consumption of formaldehyde.

Also, from *Figure 79* is quite evident that the terminal Ar*C*H_2OH of oligomers such as **36-38** which resonates around 62-63 ppm in the ^{13}C NMR spectra, are completely absent in the reaction mixture, testifying that when they form, they immediately react to give higher oligomers of type **39** or **40** or the cyclic calixarenes structures.

In conclusion the ^{1}H NMR spectra of the linear oligomers were also compared to those present in the more polar fractions eluted from the column. Unfortunately, there are no similarities or common peaks, therefore suggesting that these products are not linear oligomers. It is possible to hypothesise that these compounds are indeed particular calix[n]arenes such as oxa-calixarenes. Unfortunately, due to the limited quantities of such column samples it was not possible to acquire a ^{13}C NMR spectrum to verify the presence of ether linkages. Further studies need to be carried out with APPI-MS in order to try to determine which are the component of this fraction.

4.4 *p*-Dodecylcalix[n]arene-based detergents

Having determined from the work described in the previous paragraphs the composition of the reaction mixture between *p*-dodecylphenol and formaldehyde, an intense work started aimed at the preparation of detergents starting from this mixture of linear (16%) and cyclic (80%) compounds that will be simply defined from now on, *p*-dodecylcalixarenes.

To make detergents, usually organic acids are reacted with a metal base, such as a metal oxide or a metal hydroxide. In general, the reaction between the organic acid and the inorganic base is quite slow since the two reactants can hardly come into contact being soluble in different phases. A number of compounds, called promoters, are therefore used to facilitate the salt formation and the subsequent carbonation reaction.

Most of these reagents are used in combination with water, except for high-temperature overbasing reactions where water will evolve spontaneously. In such cases alcohols with high boiling points like 2-ethylhexanol and glycols such as ethylene glycol are used. The role of promoters is not completely understood. A hypothesis is that they improve contact between the base and the substrate acting as a surfactant thus to facilitating salt formation and carbonation. Not all promoters are effective for all overbasing reactions, and the most suitable one for a given system has to be find out by a trial and error process.

For the preparation of overbased detergents it is used a one-step process. In this procedure, the excess metal base is charged to the reaction. Once the neutral salt formation is complete, carbon dioxide blowing (carbonation) of the reaction is initiated. When carbon dioxide uptake stops, the reaction is considered complete and it is worked up to isolate the product.

At the end the final product is characterised by the TBN (Total Base Number) and by the free alkalinity (DBN, Direct Base Number). TBN is a measurement of the basicity of the detergent that is expressed in terms of the equivalent number of milligrams of potassium hydroxide per gram of oil sample (mg KOH/g), while the value of DBN measures the alkalinity due only to the metal hydroxide content. In fact a small amount of free metal hydroxide is desirable to stabilise the detergent. However, too high values of DBN lead to incompatibilities with other additives of the final lubricant formulation.

Other features of the final product that are monitored and characterise a detergent are the kinematic viscosity at 100°C and the turbidity. For the

former, low values of viscosity help the synthesis of the detergent in an industrial plant and favor the ductility of the additive in the formulation of the lubricant. On the other hand, turbidity must be low. Turbidity is measured in Nephelometric Turbidity Units (NTU). Higher values of NTU lead to more cloudy products.

4.4.1 Synthesis of the calixarene overbased detergents

The *p*-dodecylcalix[n]arenes mixture previously obtained was used, together with stearic acid or isostearic acid, in the synthesis of calcium-based detergents. The synthesis of the detergent was carried out in presence of long chain carboxylic acid, such as stearic acid (68%) or isostearic acid (50%), in order to reduce the final viscosity of the product. In fact, using only the *p*-dodecylcalix[n]arenes mixture the viscosity of the final detergent is too high, at the end of the process.

The mixture of macrocycles was added to a reactor containing the base oil (SN 150S), isostearic acid (or stearic acid), calcium hydroxide (lime) in excess, 2-ethylhexanol and ethylene glycol. The last two solvents are used like promoters, while the quantity of lime is determined in function of the desired basicity of the final product.

In the first step, the salification was carried out at 130°C and water was removed thanks to the water/2-ethylhexanol azeotrope using a Dean-Stark apparatus.

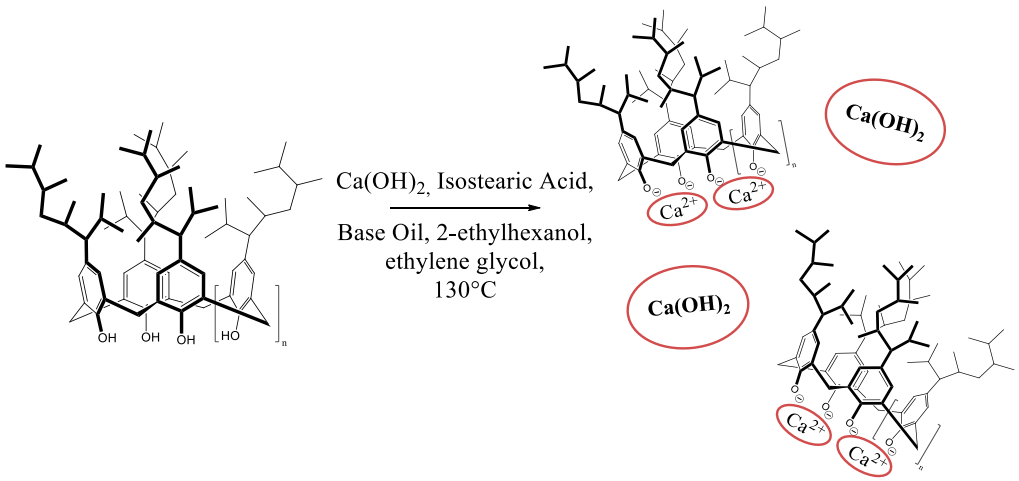


Figure 80 – Salification step of the synthesis of the overbased detergent.

In the preparation of "carboxylate" or "sulfonate" overbased detergents, the acid-base reactions with $Ca(OH)_2$ essentially leads to the complete deprotonation of all the carboxylic or sulfonate groups. However, in the case of the calixarene mixture, the situation is much less clear. The pKa values of these compounds are not readily available. For a similar compound, the *p*-sulfonatocalix[4]arenes, a pK_{a1} of 3.34 was experimentally determined for the first hydroxyl group.[19] The low value of the pKa is due to the stabilisation of the monoanion by strong hydrogen bonds with the adjacent hydroxyl groups. The second hydroxyl groups instead has a pK_{a2} of 11.5. So for these reasons, these conditions seem to lead to a partial and not to a complete salification of the phenolic OH groups. It was established by an experimental salification with calcium hydroxide of *p*-dodecylcalix[n]arenes mixture, without the carboxylic acid (stearic or isostearic), that the average degree of salification of the macrocycles is 17.1% (one phenol for a calix[6]arene or 1.4 phenols, on average, for a calix[8]arene). This evaluation was made determining the

TBN of the final product, and the DBN that is a measure of the free calcium hydroxide. The result of this step is a mixture of the calcium calixarene salts, called “calixarate”, and of the isostearate salts.

After the end of the first phase, the calcium hydroxide in excess was converted into calcium carbonate by bubbling a weighted amount of CO_2 into the reaction mixture. The carbonation step was performed at 130°C in a range of time between one and three hours depending on the desired alkalinity of the final product. The carbon dioxide was added to the reaction mixture with a suitable rate to favor its complete adsorption. Moreover, to achieve a complete adsorption of CO_2, it is important to ensure the presence of a proper amount of ethylene glycol that acts as a promoter of the reaction. Ethylene glycol is therefore added two times, at the beginning of the reaction and before the carbonation. The benefit of this approach is that it is possible to maintain the proper concentration of the reagents, in fact part of the ethylene glycol is removed with water during the salification step.

The water formed during the carbonation step is collected by distillation, and, at the end, the temperature is increased from 130°C to 200°C in order to remove all the solvents under reduced pressure.

The last stage of the synthesis is the purification. In general, the final product is filtered to remove the inorganic particles present in the mixture. The filtration step is very critical from an industrial point of view, so it is important to have products with good viscosity to facilitate this phase. However, the direct filtration of the product is not possible because the high quantity of solid impurities clog the filter blocking the process. To solve the problem, the product is diluted with xylene and a centrifugation

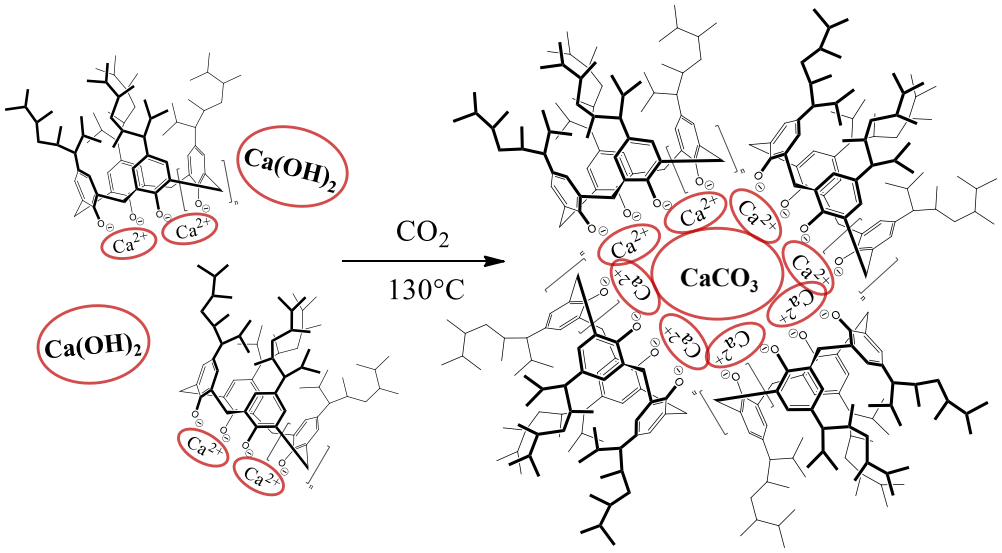


Figure 81 – Carbonation step of the synthesis of the overbased detergent.

step is performed. After this the product is filtered and the solvent is removed under reduced pressure.

The final result is a base oil containing reverse micelles of the detergent, such as in *Figure 81*. The central core is constituted by amorphous $CaCO_3$,[20] while the organic calcium soap, formed by the isostearate and by the calixarate, keeps the inorganic carbonate nuclei in solution thanks to the lipophilic tails pointing towards the oil and the polar moieties pinting towards the inorganic particles.

4.4.2 Properties of the final overbased detergent

In *Table 4* are reported the main characteristics of three formulations of overbased detergents synthesised through the *p*-dodecylcalix[n]arenes mixture and the stearic or isostearic acid. The overbased detergent **D1** contains stearic acid (68%) and it was synthesised to reach a value of about 250 of TBN. Detergents **D2** and **D3** instead contains isostearic acid (50%) and they were synthesised to reach a value of 300 of TBN.

Based on the results obtained, it is possible to calculate the efficiency of incorporation of calcium into the detergent composition from the ratio of calcium quantity introduced in the reaction mixture as calcium hydroxide and the calcium content of the final detergent. Moreover, considering that the stearic and isostearic acid are fully salified by the calcium hydroxide while the calixarene is partially salified (17.1 %), it is possible to calculate the percentage of calcium stearate or isostearate, the percentage of calcium salts of the calixarene products and the total amount of organic calcium salts (total soap).

Detergent **D1** was synthesised with the stearic acid in order to decrease the viscosity of the product and to decrease the final cost of the product. What can be clearly seen from the table is the good capacity of incorporation of the calcium that leads to the possibility to achieve high values of TBN.

It must be said that with the increasing of the TBN, the capacity of incorporation of the calcium decreases.

Attempts to synthesise detergents with stearic acids and calixarenes with higher values of TBN (results not shown) yielded products with a viscosity too high to be proposed in a lubricant. For this reason, detergents

	Detergent D1	Detergent D2	Detergent D3
Alkyl Carboxylic Acid	Stearic Acid	Isostearic Acid	Isostearic Acid
Ratio between calixarene and alkyl chain acid	1:2.1	1:1	1:1
Product Characteristics:			
Calcium Content (% wt)	9.02	10.27	10.59
Viscosity at 100°C (cSt)	55.6	80.5	61.5
TBN (mg KOH/g)	252.5	290.5	299.3
Free Alkalinity (mg KOH/g)	-	15.3	35.3
Turbidity (NTU)	4.8	4.2	2.9
Results:			
Filtration	quick	slow	slow
Incorporation eff. of Ca (%)	98.7	93.7	97.3
Calcium Hydroxide Carbonation (%)	-	94.0	86.7
Calcium stearate or isostearate (% wt.)	31.1	23.1	17.5
Calcium calixarate (% wt.)	2.6	4.0	3.0
Soap content (% wt.)	33.7	27.1	20.5

Table 4 – Characterisation of calixarene-based detergents.

D2 and **D3** were synthesised together with isostearic acid. The use of isostearic acid, in place of stearic acid, makes it possible to obtain products with significantly lower viscosity. Moreover, the combination of *p*-dodecylcalix[n]arenes and isostearic acid leads to the formation of products characterised by high content of calixarene products, good efficiency of incorporation of calcium and low viscosity values as illustrated in *Table 4*.

For the purpose to achieve overbased detergents with a lower content of soap, in detergent **D3** the ratio between the isostearic acid/calixarene amount and the base oil amount was reduced respect to **D2** (see *Table 4*, soap content, %).

Products characterised, like **D3**, by a high TBN value but a lower soap content, are desirable because they can be used together with detergents characterised by higher soap content and lower TBN.

In a lubricant it is, in fact, preferred to use such a combination rather than a single detergent with high soap content, since this formulation affords a greater flexibility to the lubricants.

In addition to this, in detergent **D3** it was used a lower molar ratio between carbon dioxide and the calcium hydroxide. In this way, using also a proper feed rate of the CO_2, it is possible to obtain lower values of percentage of calcium hydroxide carbonation (see *Table 4*) thus leading to more stable products with higher efficiency of calcium incorporation in the form of amorphous calcium carbonate in the core of the reverse micelles. In the meanwhile, the formation of crystalline calcium carbonate, which is insoluble and precipitates in the oil, is cancelled or consistently limited.

A step forward to the real lubricant was subsequently done by introducing also the remaining additives to the oil formulation. With the purpose of testing the calixarene based detergents in automotive lubricants, in fact, two lubricants (**L1** and **L2**) complete in every additive were prepared. Lubricants **L1** and **L2** contain respectively the detergents **D1** and **D2** in a concentration equals to 1.07% by weight. It was also prepared a comparative lubricant (**L3**) containing conventional detergents, in particular a combination between a detergent with low alkalinity based on calcium alkylbenzenesulfonate (TBN = 24 mg KOH/g, calcium = 2.8% wt, calcium sulfonate = 49% wt) and an overbased detergent based on calcium alkylbenzenesulfonate (TBN = 308 mg KOH/g, calcium = 12% wt, calcium sulfonate = 27% wt). Lubricant **L3** contains the same other additives of **L1** and **L2**, in the same concentrations.

The other additives, in details are: a viscosity modifier, a pour point depressant, a dispersant, antioxidants, antiwear additives and a friction modifier. Three automotive lubricants of viscosity grade SAE 5W-30 were prepared which are composed by 78.8 % in weight of base oil (SN 150S) and 21.2 % of additives, comprising also the detergents.

The lubricants were subsequently characterised determining the following parameters: kinematic viscosity at 100°C and 40°C, viscosity index, Total Base Number (TBN) and deposits at high temperature (*Table 5*).

What emerges from *Table 5* is that the lubricant formulations, containing detergents of type **D1** and **D2**, have detergency properties better than the formulation containing the conventional sulfur detergents based on calcium alkylbenenesulfonates.

	Lubricant L1	Lubricant L2	Lubricant L3
Detergent type	**D1**	**D2**	**Commercial ones**
Lubricant 5W-30 composition:			
Base oil (wt%)	78.8	78.8	78.8
Total Additives (wt%)	21.2	21.2	21.2
Soap from detergents (calcd, wt%)	0.56	0.45	0.76
Lubricant 5W-30 properties:			
Kinematic viscosity at 40°C (cSt)	70.61	71.43	76.23
Kinematic viscosity at 100°C (cSt)	11.21	11.31	11.93
Viscosity index	152	153	153
TBN (mg KOH/g)	8.50	9.10	8.2
Calcium content (wt%)	0.148	0.168	0.162
Total deposits TEOST MHT (mg)	**15.2**	**18.1**	**19.2**

Table 5 – Characterisation of the lubricants.

This behavior is determined by the TEOST MHT (Thermo-Oxidation Engine Oil Simulation Test) in the last
line, which is used for evaluating the engine oil capacity of controlling the formation of deposits at medium-high temperatures. This method consists in the determination of the weight of deposits formed in oxidant conditions (air flow) as a result of recirculation of a sample of oil, containing a small amount of catalyst, through a special rod electrically heated at a temperature of 285°C. The duration of the test is 24 hours. The method determines the total deposits as the sum of the deposits on the rod and those collected on a filter after filtration of the oil and washing with a solvent.

The lubricant formulations **L1** and **L2**, containing detergents of type **D1** and **D2**, lead to a lower formation of deposits compared to **L3**, that was prepared using the commercial detergents containing sulfur.

4.5 Conclusion

This project was undertaken to design new sulfur-free surfactants based on calixarenes and evaluate their potentials as soaps in overbased detergents for lubricant applications.

This study could conclude that *p*-dodecylphenol is a good starting material for the synthesis of new lipophilic calix[n]arenes able to be soluble in very apolar solvents such as mineral oil. Moreover, it has provided a deeper insight into the synthesis of calix[n]arenes with very long and branched chains at the upper rim.

Due to the inhomogeneous chains of the macrocycles, the separation was quite difficult. It was however possible to achieve the separation and the characterisation of the main components of the mixture. It was not possible to acquire information on the most polar fractions eluted from the column, but the analyses of these samples, aimed at collecting data on the nature and structure of these compounds, will be repeated in the next future also with the aid of APPI-MS.

The whole reaction mixture, composed of 80% calix[n]arenes and 20% linear oligomers and unreacted PDP as starting materials was used for the synthesis of the overbased detergents and the resulting detergents were used in the formulations of lubricants. These lubricants were compared with conventional sulfur-containing detergents and the data collected from performance studies showed that the calixarene overbased detergents are able to limit the formation of deposits in a comparable or even better way than commercial lubricants.

4.6 Experimental Part

General Information: All moisture sensitive reactions were carried out under nitrogen atmosphere, using previously oven-dried glassware. All dry solvents were prepared according to standard procedures, distilled before use and stored over 3 or 4 Å molecular sieves. Most of the solvents and reagents were obtained from commercial sources and used without further purification. Analytical TLC were performed using prepared plates of silica gel (Merck 60 F-254 on aluminum) and then, according to the functional groups present on the molecules, revealed with UV light or using staining reagents: $FeCl_3$ (1% in H_2O/CH_3OH 1:1), H_2SO_4 (5% in EtOH), ninhydrin (5% in EtOH), basic solution of $KMnO_4$ (0.75% in H_2O). Reverse phase TLC were performed by using silica gel 60 RP-18 F-254 on aluminum sheets. Merck silica gel 60 (70-230 mesh) was used for flash chromatography and for preparative TLC plates. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AV300 and Bruker AV400 spectrometers (observation of ^{1}H nucleus at 300 MHz and 400 MHz respectively, and of ^{13}C nucleus at 75 MHz and 100 MHz respectively). All chemical shifts are reported in part per million (ppm) using the residual peak of the deuterated solvent, which values are referred to tetramethylsilane (TMS, $\delta = 0$), as internal standard. All ^{13}C NMR spectra were performed with proton decoupling. Electrospray ionisation (ESI) mass analyses were performed with a Waters spectrometer. Atmospheric pressure photoionisation (APPI) mass analyses were performed with a Agilent 1100 series LC MSD TRAP spectrometer. Matrix assisted laser desorption/ionisation (MALDI) mass analysis were performed with a AB

SCIEX MALDI TOF 4800 Plus spectrometer. Melting points were determined on an Electrothermal apparatus in closed capillaries.

_p_-dodecylcalix[4,5,6,7,8]arenes

To a 250 ml three-neck round-bottom flask, equipped with Dean-Stark condenser, mechanical stirrer and nitrogen source, *p*-dodecyl-phenol (47.5 g, 180.9 mmol), sodium hydroxide (0.9 g, 22.5 mmol) and formaldehyde in water solution 36.7% w/w (18.2 g, 222.51 mmol) were added. The mixture was heated to 120°C and stirred, water was collected in a Dean-Stark condenser. After 2 hours xylene (150 ml) was added to the solution and the reaction mixture was heated to 140°C and stirred for 4 hours. At the end the solution was cooled to room temperature, 1M HCl (150 ml) was added and then the organic phase was separated. The organic phase was filtered and concentrated to 77.5% by weight in xylene (46.0 g, 96%). The product was triturated in methanol in order to remove the unreacted PDP and major of the linear oligomers. Then, a rate (150 mg) of the mixture of macrocycles was purified firstly by flash chromatography (petroleum ether : diethyl ether = 99:1) to obtain less complex fractions. Secondly the fractions were separated by preparative TLC (petroleum ether : diethyl ether = 99:1) to give the p-dodecyl-calix[n]arenes of different sizes.

_p_-dodecylcalix[8]arene (29): ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.51 (bs, 8H, OH); 7.10 (bs, 16H, H_{Ar}); 4.41 (bs, 8H, ArC*H*HAr); 3.50 (bs, 8H, ArCH*H*Ar); 1.80-0.10 (bs, 200H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 146.2 (C_{Ar}); 146.2 (C_{Ar}); 128.3 (C_{Ar}); 126.4 (C_{Ar}); 40.1 ($C_{12}H_{25}$); 36.9 ($C_{12}H_{25}$); 32.5 (Ar*C*H_2Ar); 31.9 ($C_{12}H_{25}$); 29.7 ($C_{12}H_{25}$); 29.4

($C_{12}H_{25}$); 26.7 ($C_{12}H_{25}$); 22.7 ($C_{12}H_{25}$); 14.9 ($C_{12}H_{25}$); 14.1 ($C_{12}H_{25}$); 8.8 ($C_{12}H_{25}$); 8.3 ($C_{12}H_{25}$). MALDI-TOF: Mass calcd for $C_{152}H_{240}O_8$: 2193.83 Found: m/z 2148.75 [20%, $(M\text{-}5CH_2+Na)^+$]; 2163.77 [40%, $(M\text{-}4CH_2+Na)^+$]; 2177.79 [50%, $(M\text{-}3CH_2+Na)^+$]; 2191.80 [50%, $(M\text{-}2CH_2+Na)^+$]; 2205.82 [60%, $(M\text{-}CH_2+Na)^+$]; 2219.83 [60%, $(M+Na)^+$]; 2233.85 [100%, $(M+CH_2+Na)^+$]; 2247.87 [60%, $(M+2CH_2+Na)^+$]; 2262.87 [60%, $(M+3CH_2+Na)^+$]; 2275.85 [50%, $(M+4CH_2+Na)^+$]; 2289.90 [40%, $(M+5CH_2+Na)^+$]; 2303.92 [20%, $(M+6CH_2+Na)^+$]; 2316.92 [20%, $(M+7CH_2+Na)^+$]. M.p.= 90.5-93.5°C. White solid.

***p*-dodecylcalix[6]arene (32):** ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.42 (bs, 6H, OH); 7.05 (bs, 12H, H_{Ar}); 4.19 (bs, 6H, ArC*H*HAr); 3.57 (bs, 6H, ArCH*H*Ar); 1.80-0.10 (bs, 150H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 147.4 (C_{Ar}); 140.8 (C_{Ar}); 126.9 (C_{Ar}); 39.9 ($C_{12}H_{25}$); 37.1 ($C_{12}H_{25}$); 33.0 (Ar*C*H_2Ar); 31.0 ($C_{12}H_{25}$); 29.7 ($C_{12}H_{25}$); 29.4 ($C_{12}H_{25}$); 26.7 ($C_{12}H_{25}$); 22.7 ($C_{12}H_{25}$); 14.2 ($C_{12}H_{25}$); 14.1 ($C_{12}H_{25}$); 8.7 ($C_{12}H_{25}$). MALDI-TOF: Mass calcd for $C_{114}H_{180}O_6$: 1645.37 Found: m/z 1641.57 [30%, $(M\text{-}2CH_2+Na)^+$]; 1655.58 [30%, $(M\text{-}CH_2+Na)^+$]; 1669.61 [50%, $(M+Na)^+$]; 1683.62 [70%, $(M+CH_2+Na)^+$]; 1697.93 [80%, $(M+2CH_2+Na)^+$]; 1711.65 [100%, $(M+3CH_2+Na)^+$]; 1725.66 [90%, $(M+4CH_2+Na)^+$]; 1739.68 [80%, $(M+5CH_2+Na)^+$]; 1767.70 [60%, $(M+6CH_2+Na)^+$]; 1782.72 [40%, $(M+7CH_2+Na)^+$]; 1796.70 [40%, $(M+8CH_2+Na)^+$]. Colourless oil.

***p*-dodecylcalix[5]arene (31):** ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.86 (bs, 5H, OH); 7.15 (bs, 10H, H_{Ar}); 4.15 (bs, 5H, ArC*H*HAr); 3.51 (bs, 5H, ArCH*H*Ar); 1.80-0.10 (bs, 125H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 147.4 (C_{Ar}); 142.9 (C_{Ar}); 140.9 (C_{Ar}); 127.0 (C_{Ar}); 126.1 (C_{Ar});

40.1 ($C_{12}H_{25}$); 38.1 ($C_{12}H_{25}$); 31.9 (ArCH$_2$Ar); 29.7 ($C_{12}H_{25}$); 29.3 ($C_{12}H_{25}$); 26.7 ($C_{12}H_{25}$); 22.7 ($C_{12}H_{25}$); 14.8 ($C_{12}H_{25}$); 8.6 ($C_{12}H_{25}$); 1.0 ($C_{12}H_{25}$). MALDI-TOF: Mass calcd for $C_{95}H_{150}O_5$: 1371.14 Found: m/z 1324.23 [60%, (M-5CH$_2$+Na)$^+$]; 1339.07 [60%, (M-4CH$_2$+Na)$^+$]; 1353.09 [60%, (M-3CH$_2$+Na)$^+$]; 1367.07 [80%, (M-2CH$_2$+Na)$^+$]; 1381.01 [90%, (M-CH$_2$+Na)$^+$]; 1395.06 [100%, (M+Na)$^+$]; 1409.10 [80%, (M+CH$_2$+Na)$^+$]; 1423.09 [80%, (M+2CH$_2$+Na)$^+$]; 1437.17 [60%, (M+3CH$_2$+Na)$^+$]; 1451.10 [40%, (M+4CH$_2$+Na)$^+$]; 1465.10 [30%, (M+5CH$_2$+Na)$^+$]. Colourless oil.

***p*-dodecylcalix[4]arene (30):** ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.23 (bs, 4H, OH); 6.96 (bs, 8H, H_{Ar}); 4.25 (bs, 4H, ArC*H*HAr); 3.50 (bs, 5H, ArCH*H*Ar); 1.80-0.10 (bs, 100H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 146.5 (C_{Ar}); 140.9 (C_{Ar}); 127.7 (C_{Ar}); 126.7 (C_{Ar}); 37.2 ($C_{12}H_{25}$); 32.6 (ArCH$_2$Ar); 31.9 ($C_{12}H_{25}$); 29.7 ($C_{12}H_{25}$); 29.4 ($C_{12}H_{25}$); 22.7 ($C_{12}H_{25}$); 14.1 ($C_{12}H_{25}$); 8.9 ($C_{12}H_{25}$); 1.1 ($C_{12}H_{25}$). MALDI-TOF: Mass calcd for $C_{76}H_{120}O_4$: 1096.21 Found: m/z 994.77 [30%, (M-9CH$_2$+Na)$^+$]; 1008.78 [50%, (M-8CH$_2$+Na)$^+$]; 1021.79 [70%, (M-7CH$_2$+Na)$^+$]; 1036.81 [80%, (M-6CH$_2$+Na)$^+$]; 1050.86 [90%, (M-5CH$_2$+Na)$^+$]; 1064.84 [90%, (M-4CH$_2$+Na)$^+$]; 1078.86 [90%, (M-3CH$_2$+Na)$^+$]; 1092.88 [90%, (M-2CH$_2$+Na)$^+$]; 1105.89 [90%, (M-CH$_2$+Na)$^+$]; 1120.85 [100%, (M+Na)$^+$]; 1133.84 [50%, (M+CH$_2$+Na)$^+$]; 1147.84 [30%, (M+2CH$_2$+Na)$^+$]; 1161.89 [20%, (M+3CH$_2$+Na)$^+$]. Colourless oil.

5-dodecyl-2-hydroxybenzaldehyde (34)

34 was synthesised according to a literature procedure.[11] To a 100 ml round-bottom flask, 10 ml of dry toluene, *p*-dodecylphenol (1 g,

3.82 mmol), tin (IV) tetrachloride (0.05 ml, 0.33 mmol) and tri-*n*-butylamine (0,4 ml, 1.53 mmol) were added. The mixture was stirred for 20 minutes at room temperature, then paraformaldehyde (0.25 g, 2.2 mmol) was added. The reaction mixture was stirred at room temperature for 8 hours and it was monitored by TLC (toluene : EtOAc = 9:1). At total consumption of the reagent, the reaction is cooled to room temperature. EtOAc (30 ml) and 1M HCl (30 ml) were added and the organic phase was separated, washed with brine (2x50 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane : EtOAc = 9.5:0.5) to give **34** as a colourless oil (0.25 g, 22%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 10.80 (s, 1H, CO*H*); 9.92 (s, 1H, OH); 7.55-7.42 (m, 2H, H_{Ar}); 6.97 (d, J = 8.4 Hz, 1H, H_{Ar}); 1.66-0.60 (m, 25H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 196.9 (*C*OH); 159.4 (C_{Ar}); 141.5 (C_{Ar}); 135.5 (C_{Ar}); 130.8 (C_{Ar}); 120.0 (C_{Ar}); 117.2 (C_{Ar}); 40.4 ($C_{12}H_{25}$); 37.0 ($C_{12}H_{25}$); 29.7 ($C_{12}H_{25}$); 29.4 ($C_{12}H_{25}$); 28.9 ($C_{12}H_{25}$); 27.2 ($C_{12}H_{25}$); 26.7 ($C_{12}H_{25}$); 23.4 ($C_{12}H_{25}$); 17.4 ($C_{12}H_{25}$); 14.9 ($C_{12}H_{25}$); 14.8 ($C_{12}H_{25}$); 14.1 ($C_{12}H_{25}$); 8.6 ($C_{12}H_{25}$); 8.3 ($C_{12}H_{25}$). ESI-MS: Mass calcd for $C_{19}H_{30}O_2$: 290.22 Found: m/z 263.17 [10%; $(M-2CH_2+H)^+$]; 277.31 [20%; $(M-CH_2+H)^+$]; 291.23 [70%; $(M+H)^+$]; 305.21 [20%; $(M+CH_2+H)^+$]; 329.34 [100%, $(M+K)^+$].

2-Hydroxymethyl-*p*-dodecylphenol (35)

35 was synthesised according to a literature procedure.[12] To a 50 ml round-bottom flask **34** (0.180 g, 0.62 mmol) and 10 ml of MeOH were added. The reaction mixture was cooled down to 0°C and $NaBH_4$

(0.047 g, 1.24 mmol) was added carefully. The reaction was stirred at room temperature for 5 hours and it was monitored by TLC (petroleum ether : diethyl ether = 1:1). At total consumption of the reagent, EtOAc (30 ml) and 1M HCl (30 ml) were added and the organic phase was separated, washed with 1M HCl (2x20 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give **35** as a colourless oil (0.15 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.28 (sb, 1H, OH); 7.19-7.12 (m, 1H, H_{Ar}); 7.03-6.93 (m, 1H, H_{Ar}); 6.82 (d, J = 8.4 Hz, 1H, H_{Ar}); 4.85 (s, 2H, C*H*$_2$OH); 2.75 (sb, 1H, CH$_2$O*H*); 1.78-0.52 (m, 25H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 153.3 (C_{Ar}); 141.7 (C_{Ar}); 140.2 (C_{Ar}); 127.7 (C_{Ar}); 125.7 (C_{Ar}); 115.8 (C_{Ar}); 64.9 (*C*H$_2$OH); 40.3 ($C_{12}H_{25}$); 37.0 ($C_{12}H_{25}$); 33.7 ($C_{12}H_{25}$); 29.7 ($C_{12}H_{25}$); 29.4 ($C_{12}H_{25}$); 29.3 ($C_{12}H_{25}$); 26.8 ($C_{12}H_{25}$); 23.5 ($C_{12}H_{25}$); 14.9 ($C_{12}H_{25}$); 14.5 ($C_{12}H_{25}$); 14.2 ($C_{12}H_{25}$); 12.3 ($C_{12}H_{25}$); 8.7 ($C_{12}H_{25}$); 8.3 ($C_{12}H_{25}$). ESI-MS: Mass calcd for $C_{19}H_{32}O_2$: 292.24 Found: m/z 275.73 [20%, $(M-3CH_2+Na)^+$]; 287.48 [20%, $(M-2CH_2+Na)^+$]; 301.45 [20%, $(M-CH_2+Na)^+$]; 315.53 [100%, $(M+Na)^+$]; 329.53 [20%, $(M+CH_2+Na)^+$]; 343.50 [20%, $(M+2CH_2+Na)^+$]; 357.54 [20%, $(M+3CH_2+Na)^+$].

2,6-Bis(hydroxymethyl)-4-dodecylphenol (36)

To a 100 ml round-bottom flask *p*-dodecylphenol (1.32 g, 5.02 mmol), formaldehyde solution 37 wt.% (1.7 ml, 2.17 mmol), potassium carbonate (1.06 g, 7.68 mmol) and 10 ml of distilled water were added. The reaction mixture was heated to 40°C and stirred for 3 days. The reaction was monitored by TLC (petroleum ether : diethyl ether = 1:1). At total consumption of the reagent, EtOAc (20 ml) and 1M HCl (20 ml) were

added and the organic phase was separated, washed with 1M HCl (2x20 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (toluene : EtOAc : acetic acid = 10:2:1). **36** appears as a colourless oil (0.34 g, 20%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.28 (sb, 1H, OH); 7.02-6.95 (m, 2H, H_{Ar}); 4.72 (s, 4H, C*H*$_2$OH); 3.79 (sb, 2H, CH_2O*H*); 1.69-0.56 (m, 25H, C_{12}*H*$_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 152.2 (*C*$_{Ar}$); 141.3 (*C*$_{Ar}$); 126.3 (*C*$_{Ar}$); 125.4 (*C*$_{Ar}$); 115.3 (*C*$_{Ar}$); 63.6 (*C*H$_2$OH); 44.2 (*C*$_{12}$H$_{25}$); 40.3 (*C*$_{12}$H$_{25}$); 40.0 (*C*$_{12}$H$_{25}$); 37.3 (*C*$_{12}$H$_{25}$); 37.0 (*C*$_{12}$H$_{25}$); 36.9 (*C*$_{12}$H$_{25}$); 36.0 (*C*$_{12}$H$_{25}$); 33.6 (*C*$_{12}$H$_{25}$); 29.3 (*C*$_{12}$H$_{25}$); 29.2 (*C*$_{12}$H$_{25}$); 29.0 (*C*$_{12}$H$_{25}$); 17.5 (*C*$_{12}$H$_{25}$); 14.9 (*C*$_{12}$H$_{25}$); 14.5 (*C*$_{12}$H$_{25}$); 14.0 (*C*$_{12}$H$_{25}$); 8.7 (*C*$_{12}$H$_{25}$); 8.3 (*C*$_{12}$H$_{25}$). ESI-MS: Mass calcd for $C_{20}H_{34}O_3$: 322.25 Found: m/z 331.48 [10%, $(M\text{-}CH_2+Na)^+$]; 345.34 [100%, $(M+Na)^+$]; 359.56 [30%, $(M+CH_2+Na)^+$]; 373.53 [10%, $(M+2CH_2+Na)^+$]; 387.57 [10%, $(M+3CH_2+Na)^+$].

3,3'-[Oxybis(methylene)]bis[5-(dodecyl)-2-hydroxy-benzenemethanol (38)

Compound **38** was separated by the crude product of **36** by flash chromatography (toluene : EtOAc : acetic acid = 10:2:1). **38** appears as a colourless oil (0.24 g, 15%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.69 (sb, 1H, OH); 8.20 (sb, 1H, OH); 7.21-6.83 (m, 4H, H_{Ar}); 4.77 (m, 8H, C*H*$_2$OH, ArC*H*$_2$OC*H*$_2$Ar); 3.56 (bs, 2H, CH_2O*H*); 1.64-0.60 (m, 50H, C_{12}*H*$_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 152.5 (*C*$_{Ar}$); 149.9 (*C*$_{Ar}$); 142.0 (*C*$_{Ar}$); 139.7 (*C*$_{Ar}$); 127.2 (*C*$_{Ar}$); 126.0 (*C*$_{Ar}$); 125.5 (*C*$_{Ar}$); 125.1 (*C*$_{Ar}$); 122.5 (*C*$_{Ar}$); 70.7 (Ar*C*H$_2$O*C*H$_2$Ar); 64.3 (*C*H$_2$OH); 40.3 (*C*$_{12}$H$_{25}$);

37.4 ($C_{12}H_{25}$); 33.6 ($C_{12}H_{25}$); 32.4 ($C_{12}H_{25}$); 30.1 ($C_{12}H_{25}$); 29.8 ($C_{12}H_{25}$); 29.5 ($C_{12}H_{25}$); 28.6 ($C_{12}H_{25}$); 27.4 ($C_{12}H_{25}$); 25.3 ($C_{12}H_{25}$); 23.5 ($C_{12}H_{25}$); 22.7 ($C_{12}H_{25}$); 20.4 ($C_{12}H_{25}$); 15.1 ($C_{12}H_{25}$); 14.3 ($C_{12}H_{25}$); 14.2 ($C_{12}H_{25}$); 12.3 ($C_{12}H_{25}$); 8.8 ($C_{12}H_{25}$). ESI-MS: Mass calcd for $C_{40}H_{66}O_5$: 626.49 Found m/z 579.60 [10%, $(M-5CH_2+Na)^+$]; 591.70 [15%, $(M-4CH_2+Na)^+$]; 607.75 [20%, $(M-3CH_2+Na)^+$]; 621.70 [30%, $(M-2CH_2+Na)^+$]; 635.76 [50%, $(M-CH_2+Na)^+$]; 649.70 [100%, $(M+Na)^+$]; 665.20 [40%, $(M+CH_2+Na)^+$]; 679.76 [40%, $(M+2CH_2+Na)^+$]; 686.81 [20%, $(M+3CH_2+Na)^+$]; 1234.23 [10%, $(2M-3CH_2+Na)^+$]; 1248.34 [15%, $(2M-2CH_2+Na)^+$]; 1262.20 [15%, $(2M-CH_2+Na)^+$]; 1276.30 [20%, $(2M+Na)^+$]; 1292.30 [15%, $(2M+CH_2+Na)^+$]; 1306.40 [15%, $(2M+2CH_2+Na)^+$]; 1318.35 [10%, $(2M+3CH_2+Na)^+$]; 1332.39 [10%, $(2M+4CH_2+Na)^+$]; 1348.66 [5%, $(2M+5CH_2+Na)^+$].

2,2'-methylenebis[4-dodecyphenol] (39)

In a 100 ml round-bottom flask, to a solution of ethylmagnesium bromide, prepared in situ from ethylbromide (0.29 ml, 3.82 mmol) and magnesium turnings (0.09 g; 3.82 mmol) in diethyl ether (5 ml), a solution of *p*-dodecylphenol (2.73 g; 0.01 mmol) in diethyl ether (10 ml) was added dropwise under stirring at room temperature. The reaction mixture was heated to 25°C and stirred for 15 hours. It was monitored by TLC (hexane : EtOAc = 9:1). At total consumption of the reagent, dichloromethane (20 ml) and 1M HCl (20 ml) were added and the organic phase was separated, washed with 1M HCl (2x20 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography

(hexane : EtOAc = 9:1) to give a mixture of **39** and **40** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.48 (sb, 1H, OH); 9.16 (sb, 2H, OH); 8.60 (sb, 2H, OH); 7.37-7.08 (m, 10H, H_{Ar}); 6.94 (bs, 4H, H_{Ar}); 4.08 (s, 6H, ArCH_2Ar); 2.03-0.42 (m, 125H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 150.0 (C_{Ar}); 147.3 (C_{Ar}); 142.9 (C_{Ar}); 140.9 (C_{Ar}); 128.5 (C_{Ar}); 126.8 (C_{Ar}); 115.3 (C_{Ar}); 40.4 ($C_{12}H_{25}$); 37.1 ($C_{12}H_{25}$); 33.8 ($C_{12}H_{25}$); 32.5 ($C_{12}H_{25}$); 32.0 (ArCH_2Ar); 30.1 ($C_{12}H_{25}$); 29.8 ($C_{12}H_{25}$); 29.5 ($C_{12}H_{25}$); 28.7 ($C_{12}H_{25}$); 27.4 ($C_{12}H_{25}$); 25.3 ($C_{12}H_{25}$); 23.6 ($C_{12}H_{25}$); 22.8 ($C_{12}H_{25}$); 20.4 ($C_{12}H_{25}$); 15.2 ($C_{12}H_{25}$); 14.5 ($C_{12}H_{25}$); 14.2 ($C_{12}H_{25}$); 12.3 ($C_{12}H_{25}$); 8.8 ($C_{12}H_{25}$). ESI-MS: Mass calcd for $C_{37}H_{60}O_2$: 536.45 Found m/z 451.67 [5%, $(M-6CH_2-H)^-$]; 465.50 [5%, $(M-5CH_2-H)^-$]; 493.50 [10%, $(M-4CH_2-H)^-$]; 697.60 [10%, $(M-3CH_2-H)^-$]; 507.40 [20%, $(M-2CH_2-H)^-$]; 520.47 [20%, $(M-CH_2-H)^-$]; 535.33 [50%, $(M-H)^-$]; 549.76 [20%, $(M+CH_2-H)^-$]; 563.36 [20%, $(M+2CH_2-H)^-$]; 577.76 [20%, $(M+3CH_2-H)^-$]; 591.59 [5%, $(M+4CH_2-H)^-$]. Mass calcd for $C_{56}H_{90}O_3$: 810.69 Found m/z 697.60 [5%, $(M-8CH_2-H)^-$]; 711.98 [5%, $(M-7CH_2-H)^-$]; 725.73 [5%, $(M-6CH_2-H)^-$]; 739.90 [10%, $(M-5CH_2-H)^-$]; 753.66 [10%, $(M-4CH_2-H)^-$]; 767.89 [20%, $(M-3CH_2-H)^-$]; 781.79 [40%, $(M-2CH_2-H)^-$]; 795.96 [50%, $(M-CH_2-H)^-$]; 809.99 [100%, $(M-H)^-$]; 823.82 [50%, $(M+CH_2-H)^-$]; 837.72 [40%, $(M+2CH_2-H)^-$]; 823.82 [50%, $(M-H)^-$]; 851.96 [40%, $(M+3CH_2-H)^-$]; 865.79 [30%, $(M+4CH_2-H)^-$]; 879.88 [10%, $(M+5CH_2-H)^-$]; 893.85 [5%, $(M+6CH_2-H)^-$].

2,6-Bis(2-hydroxy-5-dodecyl)-4-dodecylphenol (40)

40 was synthesised according to a literature procedure.[18] To a 50 ml

round-bottom flask, **36** (0.112 g, 3.36 mmol), *p*-dodecylphenol (1.12 g, 33.6 mmol), *p*-toluenesulfonic acid (0.002 g, 0.01 mmol) and 10 ml of toluene were added. The reaction mixture was heated to 110°C and stirred for 2 hours. The reaction was monitored by TLC (petroleum ether : diethyl ether = 8:2). At total consumption of the reagent, the reaction was cooled to room temperature and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether : diethyl ether = 7.5:2.5) to give **40** as a colourless oil (0.165 g, 6%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.33 (sb, 1H, OH); 8.89 (sb, 2H, OH); 7.30-7.01 (m, 6H, H_{Ar}); 6.83 (m, 2H, H_{Ar}); 3.99 (s, 4H, ArCH_2Ar); 1.60-0.69 (m, 75H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 168.0 (C_{Ar}); 143.1 (C_{Ar}); 141.1 (C_{Ar}); 128.5 (C_{Ar}); 126.9 (C_{Ar}); 125.6 (C_{Ar}); 115.6 (C_{Ar}); 40.9 ($C_{12}H_{25}$); 40.3 ($C_{12}H_{25}$); 37.0 ($C_{12}H_{25}$); 32.3 (ArCH$_2$Ar); 32.0 ($C_{12}H_{25}$); 30.6 ($C_{12}H_{25}$); 29.8 ($C_{12}H_{25}$); 29.5 ($C_{12}H_{25}$); 29.0 ($C_{12}H_{25}$); 23.9 ($C_{12}H_{25}$); 22.8 ($C_{12}H_{25}$); 19.2 ($C_{12}H_{25}$); 14.5 ($C_{12}H_{25}$); 14.2 ($C_{12}H_{25}$); 13.8 ($C_{12}H_{25}$); 8.8 ($C_{12}H_{25}$). ESI-MS: Mass calcd for $C_{56}H_{90}O_3$: 810.69 Found: m/z 697.60 [5%, $(M-8CH_2-H)^-$]; 711.98 [5%, $(M-7CH_2-H)^-$]; 725.73 [5%, $(M-6CH_2-H)^-$]; 739.90 [10%, $(M-5CH_2-H)^-$]; 753.66 [10%, $(M-4CH_2-H)^-$]; 767.89 [20%, $(M-3CH_2-H)^-$]; 781.79 [40%, $(M-2CH_2-H)^-$]; 795.96 [50%, $(M-CH_2-H)^-$]; 809.99 [100%, $(M-H)^-$]; 823.82 [50%, $(M+CH_2-H)^-$]; 837.72 [40%, $(M+2CH_2-H)^-$]; 823.82 [50%, $(M+3CH_2-H)^-$]; 851.96 [40%, $(M+4CH_2-H)^-$]; 865.79 [30%, $(M+5CH_2-H)^-$]; 879.88 [10%, $(M+6CH_2-H)^-$]; 893.85 [5%, $(M+7CH_2-H)^-$].

4.6.1 Syntheses of the detergents

General Information: The TBN (Total Base Number), expressed in mg KOH/g, was determined as described in the method ASTM D 2896. The free alkalinity (DBN) of the detergent composition, expressed in mg KOH/g, was determined as described in method ISO4314. The turbidity, expressed in nephelometric turbidity units (NTU), was determined with a HACH 2100 AN turbidimeter on the solution of the detergent composition at 5% in weight in SN 150S base oil. The calcium content was determined by inductively coupled plasma atomic emission spectrometry (ICP-AES), as described in method ASTM D 4951. The kinematic viscosity at 100°C was determined by method ASTM D 445.

The reactions were carried out in an RC-1 Mettler calorimeter consisting of a 0.5 L (or 0.25 L) jacketed five-necked glass reactor, thermostatically controlled by circulation, in the jacket, of a fluid obtained from a thermostatic bath inside the instrument. The reactor is equipped with: mechanical paddle stirrer, Dean-Stark condenser cooled with mains water, connected to a vacuum line and to a nitrogen line and equipped with a flask for collecting the distillate; bottom discharge equipped with a Teflon cock; thermocouple for temperature measurement; glass dip tube with porous septum at the end for bubbling carbon dioxide into the reaction mixture. The carbon dioxide is supplied from a cylinder fitted with a pressure reducer, placed on a balance. The flow of carbon dioxide is controlled by a mass flow meter that is connected to the cylinder and to the glass dip tube by rubber tubes. The whole system is controlled by a computer, which allows the reactor to be automated, setting the desired heating and cooling programs.

Synthesis of **D1**

To a 0.25 L reactor, equipped with mechanical stirrer, Dean Stark Condenser and nitrogen source, *p*-dodecylcalix[n]arenes at 77.5% w/w in xylene (8.68 g), stearic acid (18.04 g, 63.4 mmol) and base oil SN 150S (23.9 g) were added. The mixture was stirred and heated at 80°C for 15 minutes. Then temperature was increased to 130°C. Xylene was removed by flash distillation, cutting off the nitrogen and gradually lowering the pressure to about 20 mbar. The vacuum was released, the nitrogen atmosphere was restored and calcium hydroxide (10.45 g, 141.0 mmol) was added through a charging funnel. While stirring, 2-ethylhexanol (52.61 g, 404.0 mmol) was added to the mixture. Then, nitrogen was cut off and vacuum was applied gradually lowering the pressure until 150 mbar. The mixture was stirred at 130°C for 15 minutes. At the end the vacuum was released and the nitrogen atmoshpere was restored, ethylene glycol (3.86 g, 62.23 mmol) was added to the mixture thorugh a dropping funnel. The nitrogen was cut off and vacuum was applied gradually until a pressure of 70 mbar. The reaction was stirred and heated at 130°C for 90 minutes, during which the 2-ethylhexanol/water azeotrope was collected in the Dean-Stark condenser. After this, the vacuum was released, the nitrogen atmosphere was restored and ethylene glycol (2.80 g, 45.1 mmol) was added to the mixture. Then carbon dioxide (10.88 g, 247.0 mmol) was added at a temperature of 130°C in about 90 minutes. Then temperature was increased from 130°C to 200°C and the pressure was reduced to 60 mbar in order to remove by the solvents flash distillation. The crude product was diluted with toluene (200 ml),

centrifugated and filtered to remove the inorganic particles. The solvents was then removed under reduced pressure. The total amount is 61.9 g.
Calcium content = 9.02 % w/w
Viscosity at 100°C = 55.6 cSt
TBN = 252.2 mg KOH/g
Turbidity (5% w/w in solution of SN 150) = 4.8 NTU

Synthesis of **D2**

To a 0.5 L reactor, equipped with mechanical stirrer, Dean Stark Condenser and nitrogen source, *p*-dodecylcalix[n]arenes at 77.5% w/w in xylene (52.83 g), isostearic acid (41.02 g, 145.2 mmol) and base oil SN 150S (64.8 g) were added. The mixture was stirred and heated at 80°C for 15 minutes. Then temperature was increased to 130°C. Xylene was removed by flash distillation, cutting off the nitrogen and gradually lowering the pressure to about 20 mbar. The vacuum was released, the nitrogen atmosphere was restored and calcium hydroxide (38.28 g, 517.0 mmol) was added through a charging funnel. While stirring, 2-ethylhexanol (137.01 g, 1052.0 mmol) was added to the mixture. Then, nitrogen was cut off and vacuum was applied gradually lowering the pressure until 150 mbar. The mixture was stirred at 130°C for 15 minutes. At the end the vacuum was released and the nitrogen atmoshpere was restored, ethylene glycol (20.50 g, 330.3 mmol) was added to the mixture thorugh a dropping funnel. The nitrogen was cut off and vacuum was applied gradually until a pressure of 70 mbar. The reaction was stirred and heated at 130°C for 90 minutes, during which the 2-ethylhexanol/water azeotrope was collected in the Dean-Stark condenser. After this, the

vacuum was released, the nitrogen atmosphere was restored and ethylene glycol (14.8 g, 238.4 mmol) was added to the mixture. Then carbon dioxide (36.3 g, 824.8 mmol) was added at a temperature of 130°C in about 90 minutes. Then temperature was increased from 130°C to 200°C and the pressure was reduced to 60 mbar in order to remove by the solvents flash distillation. The crude product was diluted with toluene (500 ml, centrifugated and filtered to remove the inorganic particles. The solvents was then removed under reduced pressure. The total amount is 188.9 g.

Calcium content = 10.27 % w/w

Viscosity at 100°C = 80.5 cSt

TBN = 290.5 mg KOH/g

DBN = 13.5 mg KOH/g

Turbidity (5% w/w in solution of SN 150) = 4.2 NTU

Synthesis of **D3**

To a 0.5 L reactor, equipped with mechanical stirrer, Dean Stark Condenser and nitrogen source, *p*-dodecylcalix[n]arenes at 77.5% w/w in xylene (40.20 g), isostearic acid (31.22 g, 110.0 mmol) and base oil SN 150S (83.6 g) were added. The mixture was stirred and heated at 80°C for 15 minutes. Then temperature was increased to 130°C. Xylene was removed by flash distillation, cutting off the nitrogen and gradually lowering the pressure to about 20 mbar. The vacuum was released, the nitrogen atmosphere was restored and calcium hydroxide (38.28 g, 517.0 mmol) was added through a charging funnel. While stirring, 2-ethylhexanol (107.10 g, 822.4 mmol) was added to the mixture. Then,

nitrogen was cut off and vacuum was applied gradually lowering the pressure until 150 mbar. The mixture was stirred at 130°C for 15 minutes. At the end the vacuum was released and the nitrogen atmoshpere was restored, ethylene glycol (15.60 g, 251.3 mmol) was added to the mixture thorugh a dropping funnel. The nitrogen was cut off and vacuum was applied gradually until a pressure of 70 mbar. The reaction was stirred and heated at 130°C for 90 minutes, during which the 2-ethylhexanol/water azeotrope was collected in the Dean-Stark condenser. After this, the vacuum was realesed, the nitrogen atmosphere was restored and ethylene glycol (11.3 g, 190.1 mmol) was added to the mixture. Then carbon dioxide (15.5 g, 352.0 mmol) was added at a temperature of 130°C in about 90 minutes. Then temperature was increased from 130°C to 200°C and the pressure was reduced to 60 mbar in order to remove by the solvents flash distillation. The crude product was diluted with toluene (500 ml, centrifugated and filtered to remove the inorganic particles. The solvents was then removed under reduced pressure. The total amount is 190.2 g.

Calcium content = 10.59 % w/w

Viscosity at 100°C = 61.5 cSt

TBN = 299.3 mg KOH/g

DBN = 35.6 mg KOH/g

Turbidity (5% w/w in solution of SN 150) = 2.9 NTU

4.7 Bibliography

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Chapter 5

Organic Friction Reducers

5.1 Introduction

Friction Reducers (FR), or Friction Modifiers (FM), are a class of lubricant additives largely used in lubricants over the years. This kind of compounds reduces friction between two metal parts in contact with each other, and helps the transition from the static state, where the two metal parts are stationary, to the dynamic state, where they are in movement. Moreover, reducing the friction, they also reduce the heat developed from the relative movement of the two metal surfaces.

Very important is the ability of the friction reducers to improve the efficiency of the engine: friction developed by the pistons and by the other mechanical parts causes the loss of about 25% of the energy given off from the combustion of the fuels. Cut down friction between the components lead to best performances and also to both energetic and economic saving.

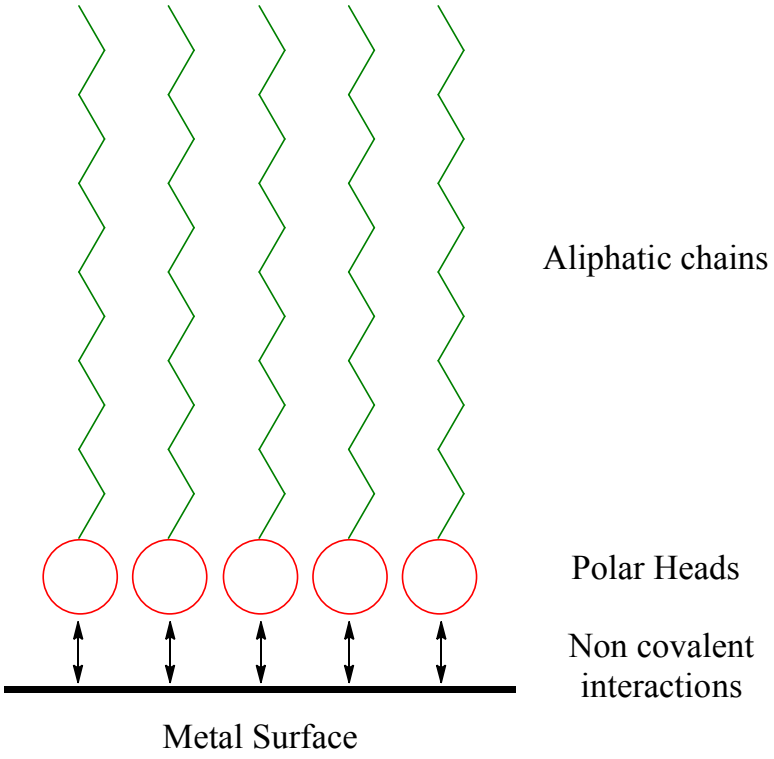


Figure 81 – Organic Friction Modifiers: formation of the monolayer.

The Organic Friction Modifiers are usually long, slim molecules characterised by a hydrophobic chain, with at least ten carbon atoms, and a polar head at one end. To the class of the friction reducers belongs: derivatives of the carboxylic acids such as stearic acids, amines, amides with long chains, phosphoric acid derivatives and organic polymers, for example, methacrylates.[1]

These additives produce a thin monolayer that covers the metal surface in contact with the lubricant. The polar heads are linked to the metal surface through non covalent interactions, while the hydrophobic chains are directed towards the oil. Thanks to the van der Waals forces, the hydrophobic chains interact each to the other and the molecules align side by side leading to the formation of a thin monolayer. When the

mechanical components are in movement the layer deforms its structure toning down the friction. At the end of the stress, the layer comes back to its original state.[1]

The efficiency and the thickness of the layer are influenced by different properties:

- The polar heads must create attractive interactions with the metal surface.
- Longer chains lead to the formation of thicker films. Moreover, with longer chains the van der Waals interactions are enhanced.
- Linear alkyl chains promote the formation of the interactions between the alkyl groups and allow the molecules to come closer thus resulting in a stronger film.
- The formation of the film has to occur at relatively low temperatures. If the temperature raise too much, the interactions between the friction reducers ant the metal surface can be broken.

5.2 Aims of Research

The objective of this research is to propose new organic molecules that can be used as friction reducers additives. The molecules suggested have a phenolic structure, and the reagent implied in their synthesis is the *p*-dodecylphenol (PDP), previously introduced in *Chapter 4*. The reason is easy to understand: the alkyl chains with a number of carbon atoms between twelve and thirteen satisfy one of the necessary requirements, that is the solubility of the additive in base oils. Moreover, PDP can again be envisaged as a simple model of calixarenes, which could be proposed as Friction Reducers in case the results of preliminary studies are encouraging.

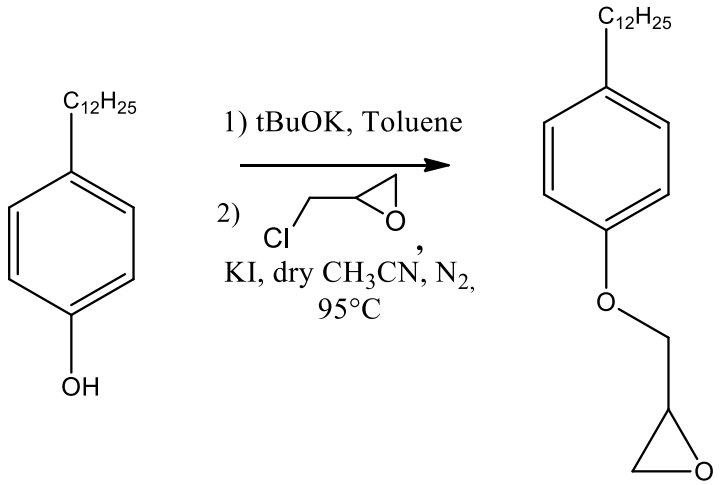
To satisfy the second fundamental characteristic for a Friction Reducer, the presence of a polar group at one end, the hydroxyl group of PDP was planned to be suitably functionalised. In a first step, the epoxy function was introduced on the PDP by using epichlorohydrin in a reaction similar to that shown in *Chapter 3*. Then the reactivity of the epoxy group towards reagents that could improve the polar nature at the end of the molecule was studied. For the reaction with the epoxide function, ethanolamine was chosen as reagent due to the presence of an effective nucleophile ($-NH_2$) and of a polar group (-OH) in its structure.

In order to evaluate if these compounds are able to reduce the friction in a proper way, they were subsequently tested and compared to a reference additive with well-known properties.

5.3 Synthesis of Friction Reducers

The *p*-dodecylphenol was functionalised with epichlorohydrin applying the same conditions used for compound **13** in paragraph *3.6* on a similar phenolic compound. The reaction was carried out at 95°C for 24 hours, monitoring it by TLC analysis and, at the end, quenching it with an aqueous solution. The use of an acid solution in the quenching was avoided to prevent the possible opening of the oxirane ring. The excess of epichlorohydrin was removed under reduced pressure together with the organic solvents and the crude product was analysed by NMR spectroscopy.

Figure 83 shows the ^{1}H NMR spectrum of compound **41**. As already seen in the previous chapter for the linear oligomers, the peaks of the hydrogens close to the inhomogeneous alkyl chain result broader and more complex respect to the other signals. Particularly in the spectrum of **41**, this effect is evident for the signals of aromatic



41

Figure 82 – Synthesis of derivative **41**.

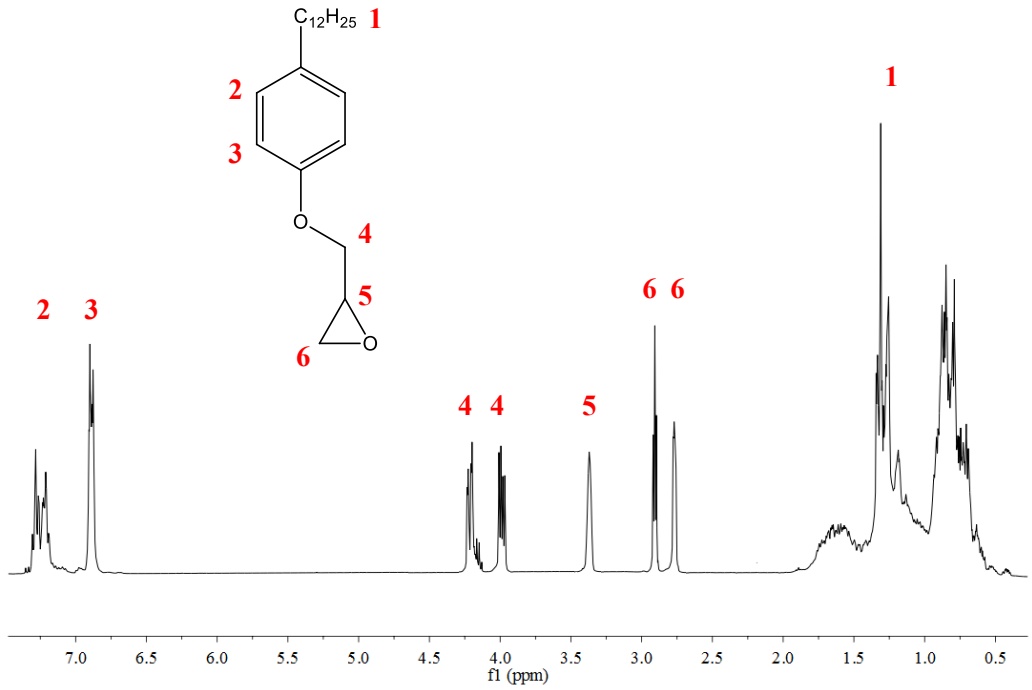


Figure 83 – ^{1}H NMR spectrum of **41** (400 MHz, $CDCl_3$, 25°C).

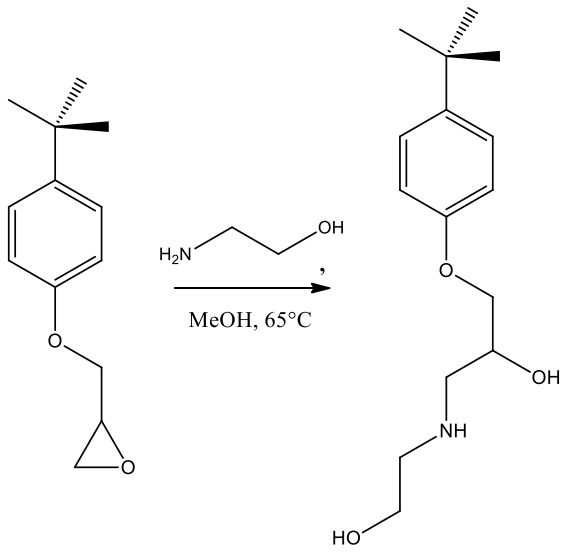
hydrogens. The well-defined doublet at 6.92 ppm belongs to the proton in ortho position to the phenyl ether bond, while the other aromatic hydrogen atoms give rise to a rather complicated signal around 7.24 ppm, arising from the superimposition of the doublets of several phenol species different in length and branches of the alkyl chains.

However, the spectrum is very similar to that one of compound **13**, the *p-tert*-butyl analogous. So by comparison with the already synthesised compound and also thanks to the ^{13}C NMR, COSY and HSQC spectra, all the signals in the spectrum were attributed. Moreover, the ratio between the values of the integrals of the aromatic signals and the values of the integrals of the aliphatic signals confirms the structure of the compound **41**. Derivative **41** was subsequently used in the following step, without any other further purifications.

5.3.1 Study of the reactivity of the epoxide group towards ethanolamine

In literature, many papers describes the reaction between styrene oxide and ethanolamine.[2–5] So, due to the similarity of the styrene oxide with compound **41**, these studies have been used as a reference for the synthesis of the target product.

The first attempt of the reaction was carried out using compound **13** because, due to the unicity of its structure, it is easier to analyse and to understand the reaction outcome. The reaction was carried out with ethanolamine (1.5 eq) in slight excess compared to **13**, using methanol as solvent. The reactive mixture was stirred and heated at 70°C for 18 hours. At the end, the TLC analysis showed the presence of several spots and the ^{1}H NMR spectrum of the crude product pointed out the presence of several impurities. The final compound was therefore purified by flash chromatography.



13 **42**

Figure 84 – Synthesis of derivative **42**.

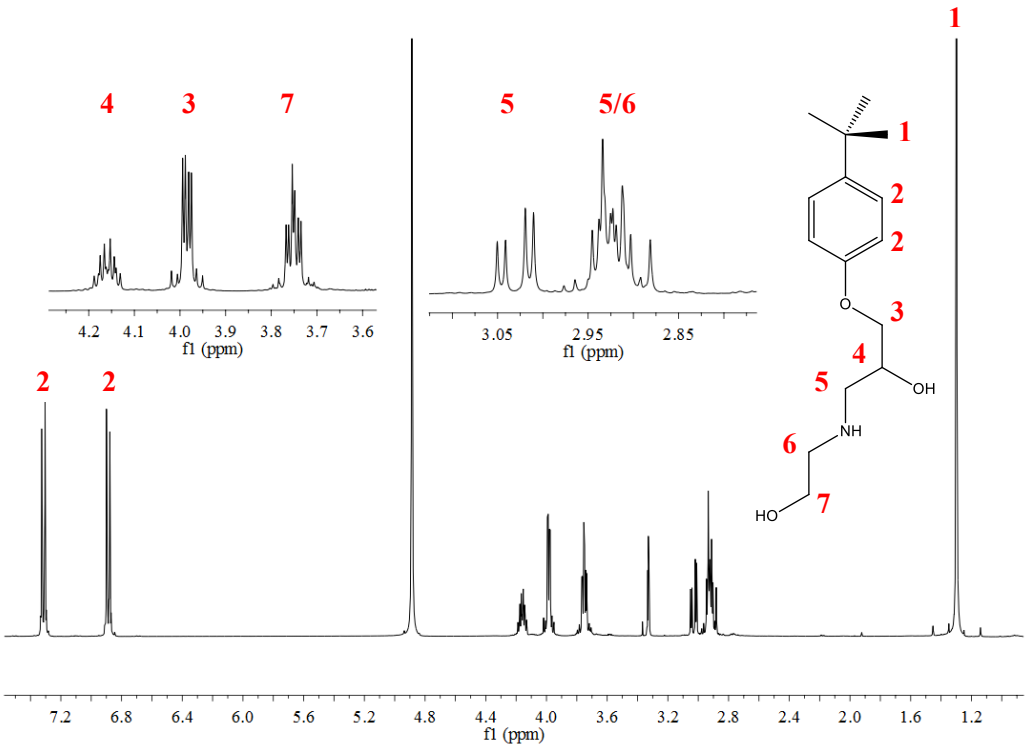


Figure 85 – ^{1}H NMR spectrum of **42** (400 MHz, CD_3OD, 25°C).

The desired product **42** was isolated and its structure was confirmed by NMR spectroscopy (*Figure 85*) and by ESI-MS. The ^{1}H NMR spectrum reveals very narrow and defined signals for the polar chain at the bottom of the molecule. Thanks to the ^{13}C NMR, COSY and HSQC spectra it was possible to attribute all the peaks. Noteworthy in this spectrum is the influence of the chiral center in position 4 on most of the signals of the polar chain. In fact, the hydrogens in position 5 are not chemical equivalent (diastereotopic) and give rise to two different doublet of doublets, one at 3.03 ppm while the other one resonates under the signal of proton 6. Moreover, this effect propagates also to the hydrogens in distant positions. For example, the signal belonging to hydrogen 7 generates a triplet of doublets at 3.60 ppm.

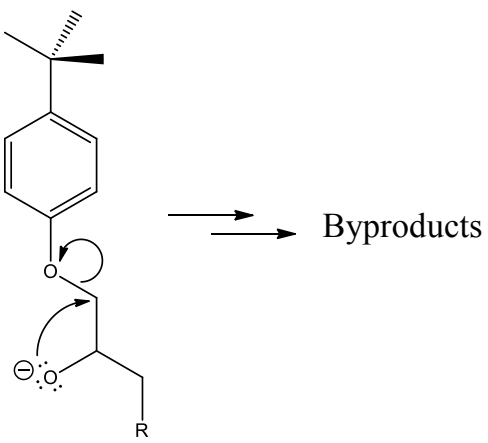


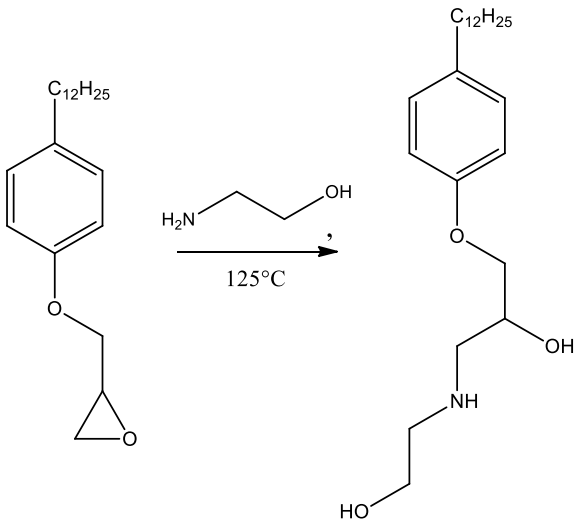
Figure 86 – Formation of byproducts (R = C_4H_9).

Interestingly, the ESI-MS analysis does not show any traces of the side reaction products discussed in *Chapter 3,* generated by the presence of an alkoxy group as a consequence of the attack of a strongly basic nucleophile (Bu^-) on the oxirane ring. As already illustrated in paragraph *3.6.1*, in presence of an alkoxide intermediate in β position to the phenol ether group, a process of elimination leads to the cleavage of the PhO-CH_2 bond with the formation of different byproducts (*Figure 86*). On the other side, in the reaction of the epoxide derivative **13** with a weaker nucleophile such as ethanolamine, such kind of side-reactions are not observed and, hence, it can conceivably be hypothesised that, after the attack of the amine on the epoxy group, there is a very fast proton transfer between the amine and the leaving alkoxide oxygen atom. In this way the alkoxide is immediately quenched and the elimination of the phenoxide is strongly discouraged.

However, the final yield of the reaction was only 25%. This low value of the yield was addressed to the possible competition of the solvent

methanol as nucleophile that could attack the epoxy group giving rise to collateral reactions.

To prevent the formation of these products, ethanolamine was directly used as solvent in the following attempt. The reaction was carried out considering the conditions of the literature.[2] Ethanolamine was heated at 125°C and then, under stirring, compound **13** was slowly added over a period of 30 minutes. After 18 hours compound **13** completely disappeared on TLCs and the reaction was stopped. In a first attempt to remove the excess of ethanolamine, the crude product was diluted in dichloromethane and washed with a diluted HCl solution. However, the final yield in compound **42** of this work-up procedure was rather low since, as could be expected, the acid solution favors also the transfer of the desired product in water. Ethanolamine alternately was removed from the crude product by vacuum distillation at 150°C, being its boiling point 175°C at atmospheric pressure. At the end, the ^{1}H NMR spectrum of the



41 **43**

Figure 87 – Synthesis of derivative **43**.

product confirmed the successful outcome of the purification, although some traces of ethanolamine could still be observed. However the final product was considered sufficiently pure. Distillation was therefore established to be the best method of separation and purification for this compound with a final yield of 50%.

The reaction conditions thus developed for compound **42**, where therefore applied also to the *p*-dodecyl derivative **41** for the synthesis of the target friction reducer **43**. Compound **41** was slowly added to the solution of ethanolamine at 125°C and the reaction was stirred at this temperature for 24 hours. Then vacuum was applied and ethanolamine was removed by distillation raising the temperature to 150°C. The obtainment of compound **43** was confirmed by the ^{1}H NMR spectrum and by ESI-MS analysis.

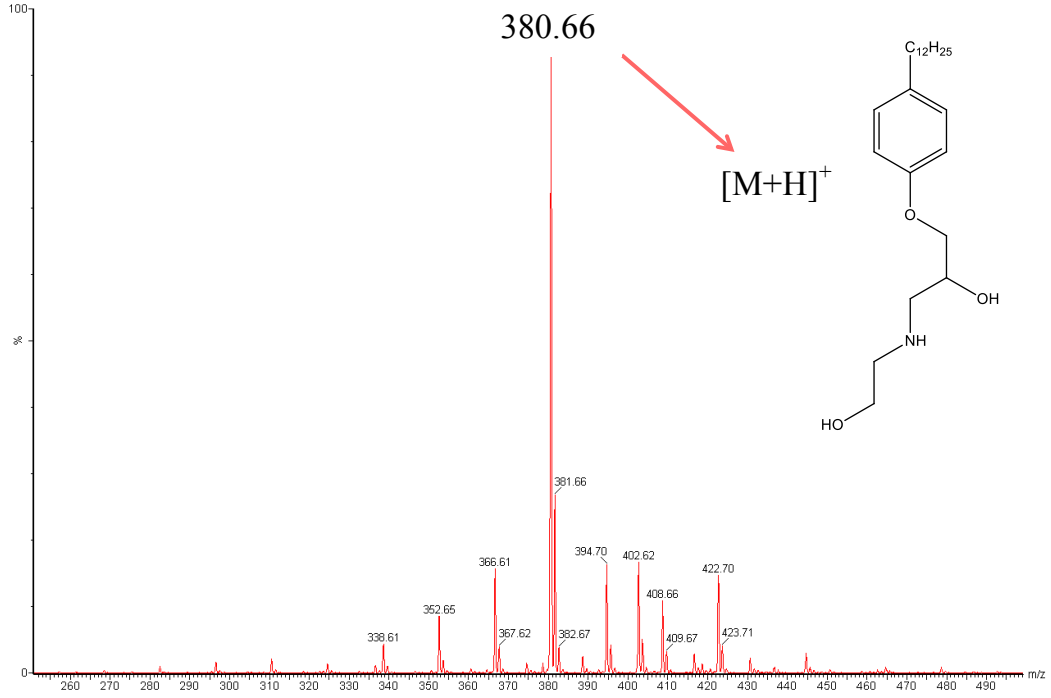


Figure 88 – ESI-MS spectrum of **43**.

The ^{1}H NMR spectrum of **43** is very similar to that in *Figure 83*, but it is characterised by very broad signals, once again, due to the great variability of the alkyl chain.
The proper outcome of the reaction was also pointed out by the ESI-MS spectrum in *Figure 88*. The base peak belongs to the $[M+H]^{+}$ adduct of **43**. Moreover, the distribution of peaks characterised by molecular weights differing of 14 amu (CH_2 units), typical for PDP derivatives is also observed.

5.4 Friction properties of the new compounds

In order to evaluate the behavior of friction reducers, both the compound **41** and **43** were used at a concentration of 1% w/w in an automotive lubricant characterised by a 0W-20 SAE Grade and with the following formula:

- Base Oils: 85.7 % w/w
- Viscosity Modifiers + Pour Point Depressant: 3,0 % w/w
- Package of additives: 10.3 % w/w
- Friction Reducer: 1 % w/w

Moreover, to compare the results of the two derivatives, it was prepared another formulation containing commercial GMS (glycerol monostearate), a well-known friction reducer taken as reference. The structure of GMS is represented in *Figure 89*. GMS is characterised by a long linear chain at

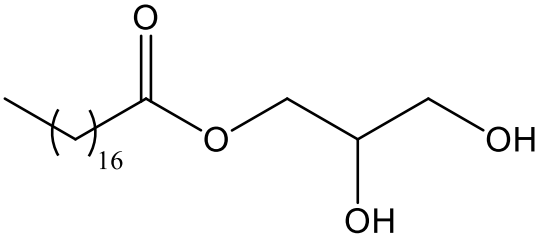


Figure 89 – Structure of GMS.

one end and this helps its solubility in mineral oil. At the other end is present a glycol moiety that interacts with the metal surface.

To test the compounds it was adopted a tribology test performed with the UTF (Ultra-Thin Film Measurement System) apparatus for measuring the friction coefficient and the film thickness of lubricants in different lubrication regimes.

The test exploit a system consisting of a coupling formed by a steel sphere loaded against a steel disc. The ball and the disc, as illustrated in *Figure 90*, rotate in two orthogonal directions and this movement generates the friction between the two objects. In this coupling, contact pressures and shear rates can reach high values, very similar to those found, for example, in gears, rolling bearings and cams. The ball is dipped in the lubricant where there is the friction reducer. Thanks to the rotational movement of the ball, between the two objects, there is the formation of a film of lubricant.

Among its multiple applications, UTF apparatus is able to qualitatively predict fuel economy of lubricants through the measure of friction coefficient (COF): smaller COF value corresponds to low energy loss.

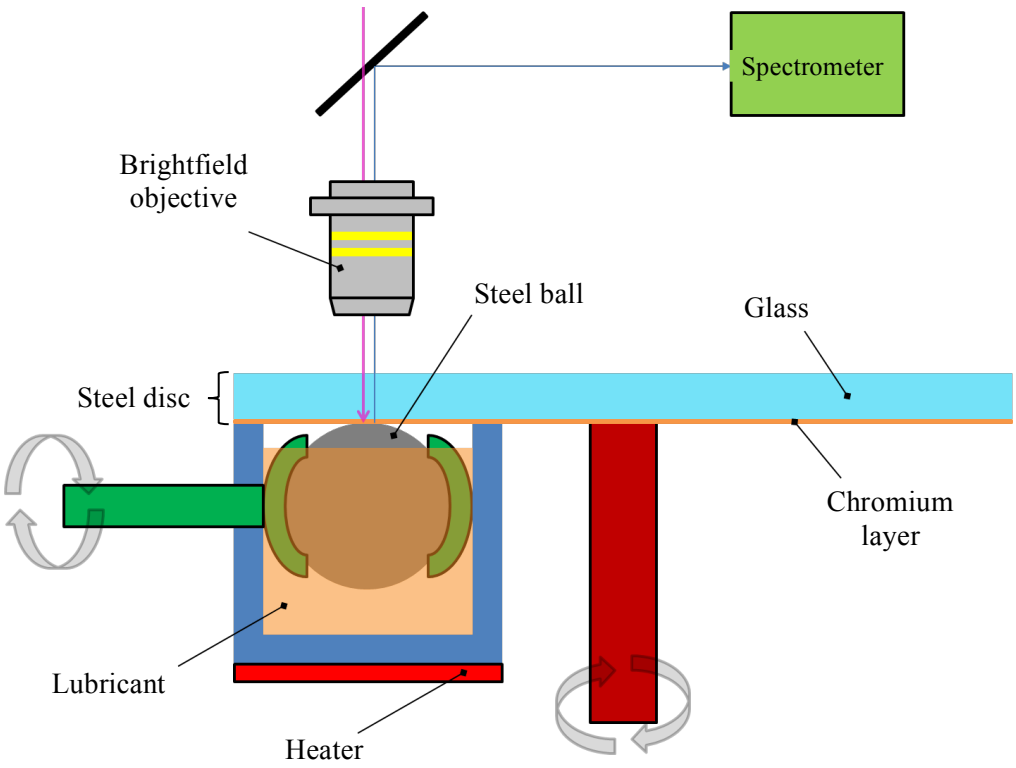


Figure 90 – UTF traction measurement coupling (scheme).

COF values are obtained as a function of entrainment speed, keeping constant the value of load, sliding/rolling ratio and temperature.

In order to better discriminate additives efficiency, tests were performed at 120°C and with a load of 30 N, sliding rolling ratio of 50% and sliding velocity range from 2 m/s to 0.004 m/s.

The friction coefficients in *Table 6* are related to different rotational speeds of the ball. In fact at very high speeds the instrument reproduces a regime of hydrodynamic lubrication in which the friction coefficient is influenced mainly by the viscosity of the lubricant. Instead at low speeds of the ball, the instrument generates a regime of boundary lubrication in which the film of the lubricant is very thin. Under the latter conditions the

Friction Coefficient at a speed of	Compound 41	Compound 43	Reference GMS
2 m/s	0.018	0.023	0.017
0.2 m/s	0.032	0.036	0.041
0.02 m/s	**0.083**	**0.101**	**0.091**
0.004 m/s	**0.108**	**0.116**	**0.092**

Table 6 – Results of the UTF (T=120°C, Load=30 N, Slide/Roll=50%).

friction coefficient is influenced by the properties of the friction reducer dissolved in the lubricant.

Having defined the origin of the data in *Table 6*, it is now possible to evaluate the friction properties of our compounds **41** and **43**. The last two lines of the table are the most important ones since they show the results of the test at low speed (in a boundary regime as explained above).

The table reveals that there is an increase of the friction coefficients moving from the GMS to our compounds. The results of the test for compounds **41** and **43** are not so bad but they are still too far from the proper values to suggest their real possible application as friction reducers.

From the test, there is an evidence that **41** and **43** have a fair influence on the friction coefficient but much lower than that of GMS. Probably this effect comes from the inhomogeneity of the chain in the molecule. In fact, as explained in the introduction, an important feature for a friction reducer is the ability to originate van der Waals interactions between the long lipophilic chains organizing side by side the tails thus promoting the

formation of a monolayer on the metal surface. Evidently, the high variability of the *p*-dodecyl units in PDP seemingly contrasts the formation of such forces or creates, by steric hindrance, a repulsion that prevents the formation/stabilisation of a regular and compact monolayer. This data therefore suggest that branched dodecyl chains of **43** and **41** are not the ideal ones to be used in these type of additives. Certainly, however, this is not the only feature differentiating **41**, **43** and GMS, since the different behavior also deeply depends from the polar head groups and their ability to graft on the metal surface.

The higher COF obtained for compound **41** over **43**, especially evident at a ball speed of 0.004 m/s, is quite unexpected. It was in fact expected the opposite behavior also due to the presence of a polar NH moiety in **43** that should have favored the interaction with the metal surface. Besides it cannot be excluded, moreover, that the epoxy group in the compound **41** is not the real moiety operating at high temperature since, due to its high reactivity, it can be easily opened or oxidised to carbonyl compounds (at least in part).

5.5 Conclusion

The aim of this investigation was to assess the friction reducer properties of these new class of compounds synthesised from *p*-dodecylphenol also in order to evaluate a possible extension to calixarene structures.

This study has identified two compounds, **41** and **43**, that contain the two main features for a friction reducer modifier: a polar head able to interact with the metal surface and a very long chain to guarantee the solubility in oil and efficient van der Waals interactions for the stabilisation of the additive monolayer on the parts in movement. The compounds were tested with the UTF apparatus (*Figure 90*) together with GMS to evaluate and compare their friction properties. Unfortunately, the final results showed that they have a minor influence than GMS on the friction coefficient of the lubricant in the boundary regime (0.004 m/s). This finding was attributed to the great variability in the alkyl chain of the two compounds that makes difficult the formation of the thin monolayer of friction reducer. Despite its exploratory nature, this study offers some insight into the design of new molecules as friction modifiers. A further study could assess the effect of a long linear chain, instead of the branched chain of PDP, in the formation of the layer and, moreover, it could be interesting evaluate the outcome of the use of other types of polar groups. Also the use of calixarene structures could possibly be explored as they can take advantage of a multivalent effect compared to the monovalent compounds **41** and **43**, that is they can have multiple and reinforced interactions with the metal surface. This would be a fruitful research area for further works.

5.6 Experimental Part

General Information: All moisture sensitive reactions were carried out under nitrogen atmosphere, using previously oven-dried glassware. All dry solvents were prepared according to standard procedures, distilled before use and stored over 3 or 4 Å molecular sieves. Most of the solvents and reagents were obtained from commercial sources and used without further purification. Analytical TLC were performed using prepared plates of silica gel (Merck 60 F-254 on aluminum) and then, according to the functional groups present on the molecules, revealed with UV light or using staining reagents: $FeCl_3$ (1% in H_2O/CH_3OH 1:1), H_2SO_4 (5% in EtOH), ninhydrin (5% in EtOH), basic solution of $KMnO_4$ (0.75% in H_2O). Reverse phase TLC were performed by using silica gel 60 RP-18 F-254 on aluminum sheets. Merck silica gel 60 (70-230 mesh) was used for flash chromatography and for preparative TLC plates. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AV300 and Bruker AV400 spectrometers (observation of ^1H nucleus at 300 MHz and 400 MHz respectively, and of ^{13}C nucleus at 75 MHz and 100 MHz respectively). All chemical shifts are reported in part per million (ppm) using the residual peak of the deuterated solvent, which values are referred to tetramethylsilane (TMS, $\delta = 0$), as internal standard. All ^{13}C NMR spectra were performed with proton decoupling. Electrospray ionisation (ESI) mass analyses were performed with a Waters spectrometer. Melting points were determined on an Electrothermal apparatus in closed capillaries.

4-dodecyl-phenyl glycidyl ether (41)

To a 250 ml round-bottom flask, *p*-dodecylphenol (9.93 g, 37.93 mmol), potassium *tert*-butoxide (4.68 g, 41.72 mmol) and 80 ml of acetonitrile were added. The mixture was stirred for 30 minutes, then epichlorohydrin (4.45 ml, 56.89 mmol) was added carefully. The reaction mixture was heated at 95°C and stirred for 18 hours. The reaction was monitored by TLC (hexane : EtOAc = 9:1). At total consumption of the reagent, EtOAc (100 ml) and brine (100 ml) were added. The organic phase was separated, washed with distilled water (2x100 ml), dried over anhydrous Mg_2SO_4 and the solvent was removed under reduced pressure to give **41** as an orange oil (10.9 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.35-7.19 (m, 2H, H_{Ar}); 6.90-6.87 (m, 2H, H_{Ar}); 4.17 (dd, J_1 = 3.2 Hz, J_2 = 10.8 Hz, 1H, OC*H*HCHOCH$_2$); 3.98 (dd, J_1 = 5.6 Hz, J_2 = 10.8 Hz, 1H, OCH*H*CHOCH$_2$); 3.37 (m, 1H, OCH$_2$C*H*OCH$_2$); 2.90 (t, J = 4.4 Hz, 1H, OCH$_2$CHOC*H*H); 2.77 (m, 1H, OCH$_2$CHOCH*H*); 1.81-0.60 (m, 25H, $C_{12}H_{25}$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 156.1 (C_{Ar}); 143.2 (C_{Ar}); 142.5 (C_{Ar}); 140.9 (C_{Ar}); 140.6 (C_{Ar}); 127.6 (C_{Ar}); 126.8 (C_{Ar}); 114.1 (C_{Ar}); 68.7 (O*C*H$_2$CHOCH$_2$); 50.2 (OCH$_2$*C*HOCH$_2$); 44.7 (OCH$_2$CHO*C*H$_2$); 44.4 ($C_{12}H_{25}$); 38.3 ($C_{12}H_{25}$); 37.1 ($C_{12}H_{25}$); 32.4 ($C_{12}H_{25}$); 29.4 ($C_{12}H_{25}$); 27.3 ($C_{12}H_{25}$); 26.8 ($C_{12}H_{25}$); 23.5 ($C_{12}H_{25}$); 17.5 ($C_{12}H_{25}$); 14.9 ($C_{12}H_{25}$); 14.5 ($C_{12}H_{25}$); 14.1 ($C_{12}H_{25}$); 12.3 ($C_{12}H_{25}$); 8.7 ($C_{12}H_{25}$); 8.3 ($C_{12}H_{25}$). ESI-MS: Mass calcd for $C_{21}H_{34}O_2$: 318.25 Found: m/z 589.67 [20%, $(2M+Na)^+$]; 603.78 [50%, $(2M-4CH_2+Na)^+$]; 617.82 [30%, $(2M-3CH_2+Na)^+$]; 631.54 [30%, $(2M-2CH_2+Na)^+$]; 645.91 [60%, $(2M-CH_2+Na)^+$]; 659.95 [100%, $(2M+Na)^+$]; 675.8 [50%,

$(2M+CH_2+Na)^+$]; 687.89 [30%, $(2M+2CH_2+Na)^+$]; 701.86 [20%, $(2M+3CH_2+Na)^+$]; 719.00 [10%, $(2M+4CH_2+Na)^+$].

1-(4-*tert*-butylphenoxy)-3-[(2-hydroxyethyl)amino]-2-propanol (42)

To a 100 ml round-bottom flask, ethanolamine (0.21 ml, 3.46 mmol) and 10 ml of methanol were added. Then, under vigorous stirring, **13** (0.47 g, 2.31 mmol) was added to the mixture carefully. The reaction mixture was stirred at 70°C and it was monitored by TLC (hexane : EtOAc : MeOH : = 6:4.1). At total consumption of the reagent, the reaction was cooled to room temperature and dichloromethane (30 ml) and 1M HCl (30 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane : EtOAc : MeOH : = 6:4.1) to obtain **42** as a yellow oil (0.14 g, 26%). ^{1}H NMR (400 MHz, CD_3OD) δ (ppm): 7.31 (d, J = 9.0 Hz, 2H, H_{Ar}); 6.88 (d, J = 9.0 MHz, 2H, H_{Ar}); 4.18-4.13 (m, 1H, $OCH_2CHOHCH_2NH$); 3.98 (dd, 2H, J_1 = 2.4 Hz, J_2 = 5.3 Hz, $OCH_2CHOHCH_2NH$); 3.75 (td, J_1 = 2.3 Hz, J_2 = 5.5 Hz, 2H, $NHCH_2CH_2OH$); 3.03 (dd, J_1 = 3.7 Hz, J_2 = 12.4 Hz, 1H, $OCH_2CHOHCHNH$); 2.94-2.88 (m, 3H, $OCH_2CHOHCHNH$, $NHCH_2CH_2OH$); 1.30 (s, 9H, $C(CH_3)_3$). ESI-MS: Mass calcd for $C_{15}H_{25}NO_3$: 267.36 Found: m/z 268.33 [100%; $(M+H)^+$]; 290.30 [70%; $(M+Na)^+$].

1-(4-dodecylphenoxy)-3-[(2-hydroxyethyl)amino]-2-propanol (43)

To a 100 ml round-bottom flask, ethanolamine (12 ml, 20.00 mmol) was added and it was heated at 125°C and stirred. Then **41** (4.84 g, 15.22 mmol) was added to the mixture carefully over a period of 30 minutes. The reaction mixture was stirred at 125°C and it was monitored by TLC (EtOAc : MeOH : NEt_3 = 8.5:1:0.5). At total consumption of the reagent, the reaction was cooled to room temperature and EtOAc (100 ml) and 1M NaOH (100 ml) were added. The organic phase was separated, washed with distilled water (3x30 ml), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by vacuum distillation in order to remove the excess of ethanolamine. **43** appear as a yellow oil (2.85 g, 49%). ^{1}H NMR (300 MHz, CD_3OD) δ (ppm): 7.27-7.18 (m, 2H, H_{Ar}); 6.92 (d, J = 8.4 MHz, 2H, H_{Ar}); 4.43-4.39 (m, 1H, $OCH_2C\mathit{H}OHCH_2NH$); 4.11-4.00 (m, 2H, $OC\mathit{H}_2CHOHCH_2NH$); 3.92 (t, J = 5.1 Hz, 2H, $NHCH_2C\mathit{H}_2OH$); 3.42 (dd, J_1 = 2.7 Hz, J_2 = 12.6 Hz, 1H, $OCH_2CHOHC\mathit{H}HNH$); 3.33-3.24 (m, 3H, $OCH_2CHOHCH\mathit{H}NH$, $NHC\mathit{H}_2CH_2OH$); 1.75-0.60 (m, 25H, $C_{12}\mathit{H}_{25}$). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 156.2 (C_{Ar}); 142.8 (C_{Ar}); 142.0 (C_{Ar}); 140.0 (C_{Ar}); 127.8 (C_{Ar}); 113.8 (C_{Ar}); 69.8 ($OC\mathit{H}_2CHOHCH_2NH$); 65.4 ($OCH_2\mathit{C}HOHCH_2NH$); 56.6 ($NHCH_2\mathit{C}H_2OH$); 50.04 ($OCH_2CHOH\mathit{C}H_2NH$); 49.8 ($NH\mathit{C}H_2CH_2OH$); 40.0 ($\mathit{C}_{12}H_{25}$); 37.2 ($\mathit{C}_{12}H_{25}$); 36.8 ($\mathit{C}_{12}H_{25}$); 32.0 ($\mathit{C}_{12}H_{25}$); 29.6 ($\mathit{C}_{12}H_{25}$); 28.9 ($\mathit{C}_{12}H_{25}$); 28.8 ($\mathit{C}_{12}H_{25}$); 26.3 ($\mathit{C}_{12}H_{25}$); 21.5 ($\mathit{C}_{12}H_{25}$); 17.2 ($\mathit{C}_{12}H_{25}$); 14.2 ($\mathit{C}_{12}H_{25}$); 13.8 ($\mathit{C}_{12}H_{25}$); 13.5 ($\mathit{C}_{12}H_{25}$); 11.6 ($\mathit{C}_{12}H_{25}$); 8.0 ($\mathit{C}_{12}H_{25}$); 7.7 ($\mathit{C}_{12}H_{25}$). ESI-MS: Mass calcd for $C_{22}H_{41}NO_3$: 379.310 Found: m/z 352.65 [10%;

$(M-2CH_2+H)^+$]; 366.61 [20%; $(M-CH_2+H)^+$]; 380.27 [100%; $(M+H)^+$]; 394.70 [20%; $(M+CH_2+H)^+$]; 402.34 [20%, $(M+Na)^+$]; 408.66 [10%, $(M+2CH_2+H)^+$]; 422.70 [10%, $(M+3CH_2+H)^+$].

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