The potential industrial applications of calixarenes

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Abstract
Calixarenes can be considered as macrocycles or perfectly defined cyclic oligomers. Their potentiel applications, determined from industrial chemistry publications and existing patents are presented. Non modified calixarenes and calixarenes modified by chemical reactions are successively taken into account. The latter may be considered as "molecular platforms" to which functional groups are fixed. The described applications concern, recovery of caesium and uranium, lanthanide sequestration, separation of neutral organic molecules, stabilizers for organic polymers, pollution control selective complexation of neutral cations, phase transfer agents, accelerators for instant adhesives, ion scavengers for electronic devices, Langmuir-Blodgett film and membranes, catalytic properties.

Calixarenes are macrocycles resulting from alternate associations of phenolic and methylenic groups. Different substituents can replace the hydrogen atoms present in these different groups. The following macrocycles are examples of calixarenes.

Paraisopropylcalix[8]arene *Tetraethylether of calix[4]arene* *Parahydroxycalix[6]arene*
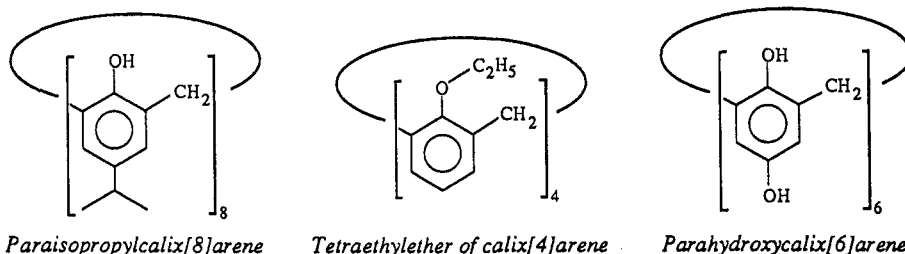
The methylene group can itself be substituted or replaced by other groups such as -CH$_2$-O-CH$_2$-. This gives rise to oxacalixarenes such as the following bis-homooxacalix[4]arene.

Homooxacalix[4]arene
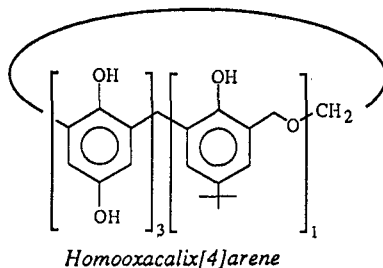
There are numerous other possibilities to obtain new calixarenes. This demonstrates the wealth of this class of products and the possibilities to obtain substances with interesting properties.

Furthermore calixarenes are characterized by a set of specific properties for example :

- well defined oligomer,
- large thermal stability as phenoplasts,
- good chemical stability as phenoplasts,
- very high melting points,
- very low solubility in many solvents and good solubility in certain solvents,
- possible functionalization,
- good flexibility of many calixarene molecules,
- large variety of calixarene molecules with various sizes of cavities,
- good properties of complexation with metals and neutral molecules,
- good properties of selective complexation,
- not very expensive macrocycles compared with crown-ethers and cryptates, and high-value products as compared with phenoplasts.

Calixarenes can be considered from two points of view : either as **macrocycles** in the same way as crown ethers and cryptates, in which case they are notably relevant to supramolecular chemistry, or as perfectly defined **cyclic phenolic oligomers**, in which case they are relevant to macromolecular chemistry.
Potential applications of calixarenes determined from industrial chemistry publications and existing patents will be presented within the framework of supramolecular and macromolecular chemistry without distinction.
Certain studies have already been analysed up to 1988 (ref. 1 and 2). Since this date other publications and patents have appeared.
By taking into account all this available information, we will present the main applications of calixarenes, with the help of selected examples.
Firstly, applications of non modified calixarenes will be described. In a second part, calixarenes modified by chemical reactions will be presented. According to Reinhoudt (ref. 3), such calixarenes can be considered as "molecular platforms" to which functional groups are fixed.

1.   APPLICATIONS OF NON-MODIFIED CALIXARENES

1.1.   Recovery of caesium

The patent (ref. 4) for the recovery of caesium is the oldest concerning non modified calixarenes. This patent describes a process for recovering metallic cations, at high concentration, from solutions of nuclear waste materials. As schematically shown in figure 1, the process involves three liquid phases.
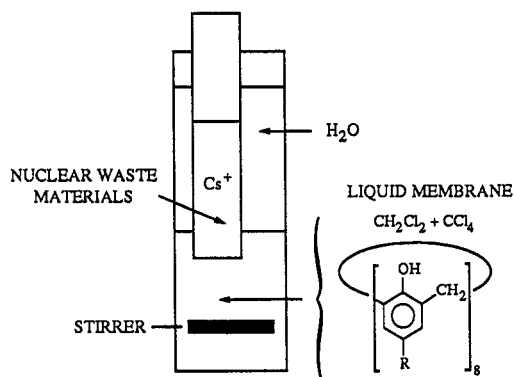

Fig. 1. Apparatus for recovery of caesium using calixarenes.

The first phase is aqueous and contains a plurality of degradation products of uranium splitting which have molecular weights of about half the molecular weight of uranium, including caesium. The second phase is made of a certain percent of dichloromethane and carbon tetrachloride. 1 mM solution of calix[8]arene is prepared with the second phase. The third phase is distilled and deionized water. The second phase acts as a liquid membrane allowing the metallic cations to migrate from the first phase to the third one.

Table 1 illustrates the relative transport rates utilising various aqueous metal hydroxides for this system, with the main result that the transport rate for Cs^+ is about 100 times higher than for K^+, Na^+, and Li^+ and 6 times higher than for Rb^+. Although no actual data are given for mixtures of metal cations in this patent, a later publication of the same authors also describes ion transport experiments with various mixtures of alkali metal ions.

The low solubility of these calixarenes in aqueous media ensures that loss from the organic membrane is minimal. However, these non modified calixarenes are also rather sparingly soluble in the organic membrane, which for effective practical devices is a rather limiting factor. The above system also works only with a rather strongly basic source phase (ref. 5), suggesting, that at least one hydroxyl proton has to be removed during the complexation of the Cs^+ cation. Thus a neutral complex is formed in the organic membrane and the system offers potential for coupling cation transport to the reverse flux of protons.

TABLE 1.
Alkaline ions transport rate for the system with p-tert-butylcalix[8]arene.

Source phase	Transport rate x 10^7 (moles / 24 h)
LiOH	0,9
NaOH	1,5
KOH	1,7
RbOH	22
CsOH	130
$Ca(OH)_2$	0,5
$Sr(OH)_2$	0,1

1.2. Lanthanide sequestration

Harrowfield et al (ref. 6) have prepared complexes of europium and other lanthanides with p-tert-butyl-calix[8]arene under basic conditions. Bunzli and Harrowfield (ref. 2 p. 211) indicate that p-tert-butyl-calix[8]arene provides a ready means of converting all the lanthanides to organic-solvent soluble complexes, suggesting that it might be used in solvent extraction and purification of the lanthanides as well as in lanthanide ion catalysis of reactions in apolar solvents. Though present indications are that the kinetics of complex formation and breakdown may be too slow for efficient solvent extraction processes, it may be possible to modify the tert-butyl substituents in such a way as to overcome this difficulty.

1.3. Stabilizers for organic polymers

The thermally stable and non volatile nature of calixarenes allow their use as antioxidants for organic polymers. Seiffarth et al (ref. 7) have shown that the non modified calixarenes were efficient inhibitors of polyolefin oxydation (figure 2). This was also demonstrated for the oxidation of tetralin
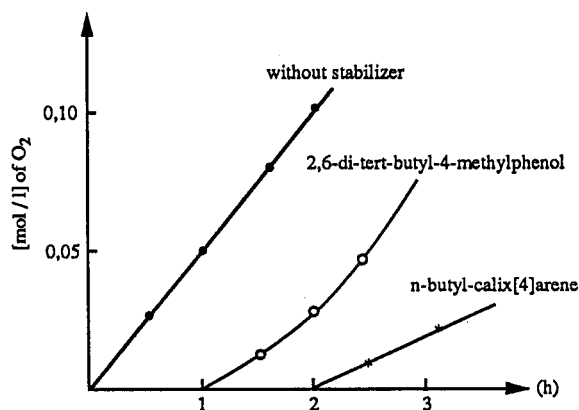

Fig. 2. Autoxidation of polyethylene (LDPE Mirathen A1 21 FA), comsumption of oxygen as a function of the reaction time.

(figure 3). In both cases improvement on the classical antioxidant 2,6-di-tert-butyl-4-methylphenol was noted. This is probably because calixarenes form relatively stable phenoxy-type radicals, which prevent propagation of radical chain reactions.
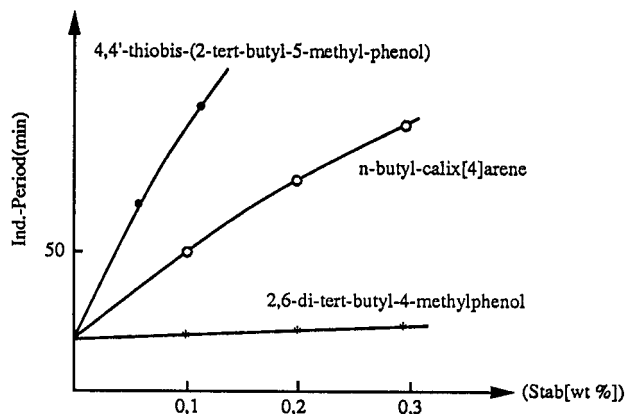

Fig. 3 - Induction periods for the AIBN initiated oxidation
of tetralin at 60 °C in the presence of different stabilizers.

Since these studies, the same authors have taken out numerous other patents in this area (ref. 8, 9, 10). These concern above all, the use of modified calixarenes in comparison to the non-modified calixarenes.

1.4. Separation of neutral organic molecules

The ability of the calixarenes to "host" neutral organic molecules has led Perrin et al (ref. 11) to use paraalkylcalixarenes for separation of the isomeric xylenes. Figure 4 shows the separation obtained on shaking a mixture consisting of equal quantities of the three xylene isomers with different calixa-renes in comparison with benzopinacol. The most striking results concern the specificity of p-isopropylcalix[4]arene for p-xylene and p-isopropylbishomooxacalix[4]arene for o-xylene. The results obtained are much better than those obtained with benzopinacol under the same conditions (ref. 12).
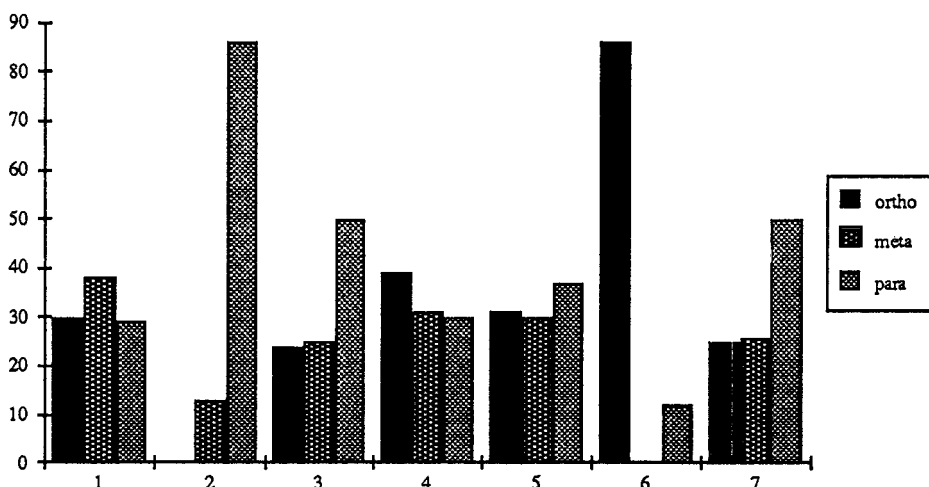

Fig. 4. Selective extraction of xylenes with different calixarenes : (1) Initial mixture, (2) p-isopropylcalix[4]arene, (3) p-tert-butylcalix[4]arene, (4) p-(1,1,3,3-tetramethylbutyl)calix[4]arene, (5) double calix[4]arene (-(CH$_2$)$_8$), (6) p-isopropylbishomooxacalix[4]arene, (7) benzopinacol.

As shown in table 2, conditions have been found to form a totally pure paraisopropylcalix[4]arene-p-xylene complex.

TABLE 2. Crystallization yields and selectivities of the supramolecular sets : paraisopropylcalix[4]arene-xylenes.

1	2	3	4	5	6	7
A1	0,020	5	77	76,6	19	4,4
A2	0,0105	5	63	81,45	15,75	2,8
A3	0,0052	5	0	---	---	--
B1	0,020	2	51	100	0	0
B2	0,020	5	77	76,6	19	4,4
C1	0,0105	5	63	81,45	15,75	2,8
C2	0,0105	17	70	82,2	15,13	2,66

(1) experiment code, (2) molar fraction of calixarene in the 1:1:1 xylene isomer mixture, (3) crystallization time (hrs), (4) % of 1 recovered, (5) % of p-xylene recovered, (6) % of m-xylene recovered, (7) % of o-xylene recovered.

The crystal structure of the supramolecules formed between paraisopropylcalix[4]arene and the different xylenes were determined. All these supramolecules are 1:1 complexes. The crystal structure of the complexes with o-xylene and m-xylene are isomorphous, crystallizing in the monoclinic group Cc, where as the crystal structure of paraisopropylcalix[4]arene-p-xylene is tetragonal (group P 4/n). In the solid state, the calixarene molecule loses its symmetry when complexed with o- or m-xylene (figure 5). However, when complexed with p-xylene, it conserves its symmetry. The symmetry axis of the p-xylene molecule coincides with the symmetry axis of the calixarene. Furthermore, due to the 4 symmetry, p-xylene can take up two different positions in the macrocycle.
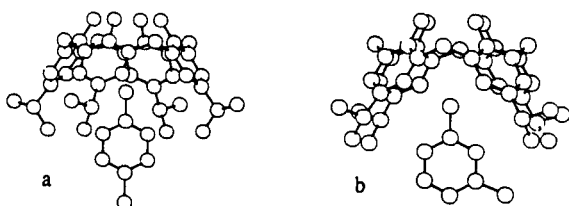

Fig. 5. View of supramolecules in the solid state. a : p-xylene, b : m-xylene.

The phenomenon of molecular recognition could be explained by the greater number of efficient approaches between the p-xylene and the calixarene in comparison to the other two isomers. This mainly results from the fact that the approach following the axis of symmetry of the p-xylene molecule is identical in both directions, which is not the case for the other two isomers.

The molecular recognition of xylenes by paraisopropylcalix[4]arene could play an important part in the industrial separation of xylenes.

Gutsche et al (ref. 13) have studied the interaction of p-allylcalix[4]arene with amines in acetonitrile. They postulate that an endocalix complex is formed in a two-step process with tert-butylamine but not with tert-pentylamine. This observation could lead to a method for the separation of amines.

1.5. Pollution control

In a recent patent Wainwright (ref. 14) proposes a method for the removal of organic compounds, particularly polar hydrocarbons such as halogenated hydrocarbons with non-solvated calixarene compounds.

The chlorination of water supplies for the purpose of improving their microbiological quality has been common practise since 1908. However, in 1974, it was discovered that an undesirable side reaction occurred within a chlorinated supply through reaction of the chlorine with naturally occurring humic and, fulvic acids that resulted in the formation of trihalomethanes. As a consequence of this, chloroform and if bromide ions are present, dichlorobromomethane, chlorodibromomethane and bromo-

form, which have carcinogenic properties are frequently encountered contaminants in water supplies for use in the home and in industry.

Wainwright has discovered that a solution of tert-butylcalix[6]arene has a remarkable propensity for sequestering trihalomethane molecules (figures 6 and 7) with high rates of reaction, yielding inclusion compounds of relatively high stability. In order to obtain high reactivity in a solid phase the calixarene compound is preferably attached to a solid support.
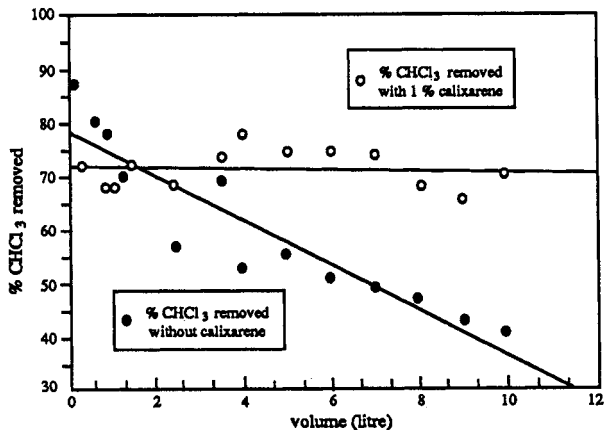
bed volume = 10 ml   loading = 1 % (w/w) receptor on filtrasorb 400 (55 mg on 55 g)
retention time = 12 seconds   receptor = t-butyl-calix[6]arene

Fig. 6.
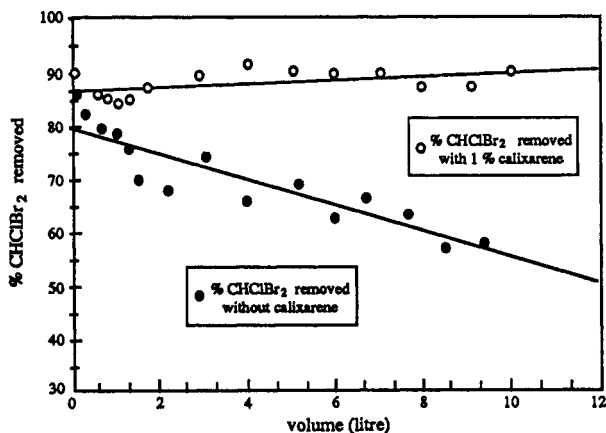
bed volume = 10 ml   loading = 1 % (w/w) receptor on filtrasorb 400 (55 mg on 55 g)
retention time = 12 seconds   receptor = t-butyl-calix[6]arene
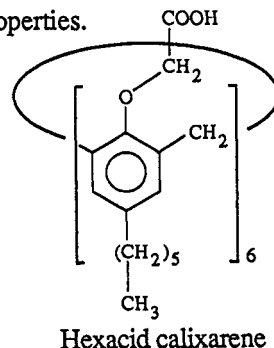
Fig. 7.

2. APPLICATIONS OF MODIFIED CALIXARENES

2.1. Recovery of uranium

Table 3 shows that modifying a calixarene, greatly modifies the extraction properties.

TABLE 3.
Extraction of uranium from aqueous solution to o-dichlorobenzene.

Compound	pH = 8.1	pH = 10.0
p-tert-butylcalix[6]arene	0.0	18.0
Hexacid calixarene	97.4	99.8
Dicyclohexyl-18-crown-6	1.3	2.1

Hexacid calixarene

It is clear that calixarenes enable the recovery of uranium. The hexacid derivative called "super uranophile" by the inventors is the most effective extractant among the modified calixarenes (ref. 15). Shinkai (ref. 16) noticed that calix[5] and calix[6]arenes have ideal architectures for the design of uranophiles, because introduction of ligand groups into each benzene unit of these calixarenes provides exactly the required pseudoplanar penta and hexacoordinate structure.

2.2. Selective complexation of metal cations

The use of non modified calixarenes in selective complexation of metal cations is severely limited by their low solubility in organic solvents and in water and their limited metal cation binding ability particularly in neutral to acid media.

Numerous variations of the residues attached to the phenolic groups of the non modified calixarenes are described in the literature and various examples are discussed by Ungaro and Pochini (ref. 2 p. 127), Schwing and McKervey (ref. 2 p. 149), and Shinkai (ref. 2 p. 173).

For instance monocarboxylic acid triester was successfully employed in selective extraction of silver from an aqueous sodium / silver picrate mixture at pH : 7 by shaking with a solution of modified calixarene I in dichloromethane (table 4). Recently McKervey et al (ref. 17) proposed new modified calixarenes and oxacalixarenes. The thioamide hexamer has an advantage over the amide in that it selectivity sequesters silver and lead over alkaline and alkali metals.

TABLE 4. Extraction of metal picrates (given in %) from aqueous solution to CH_2Cl_2 by equimolar nitrogen-containing calix[4]arene derivatives.

Compound	[a]Na^+	Cu^{2+}	Fe^{2+}	Ag^+	Au^{3+}	Hg^{2+}	Eu^{3+}	U^{4+}
I	55	5.1	48.1	63.6	36.3	30.9	6.7	29.9
II	0	11.4	44.7	77.0	---	33.6	---	24.9
III	94.6	1.8	12.1	16.2	9.2	6.8	---	6.4
18-crown-6	13.5	1.0	3.0	2.7	---	----	---	---

[a] from basic solution.
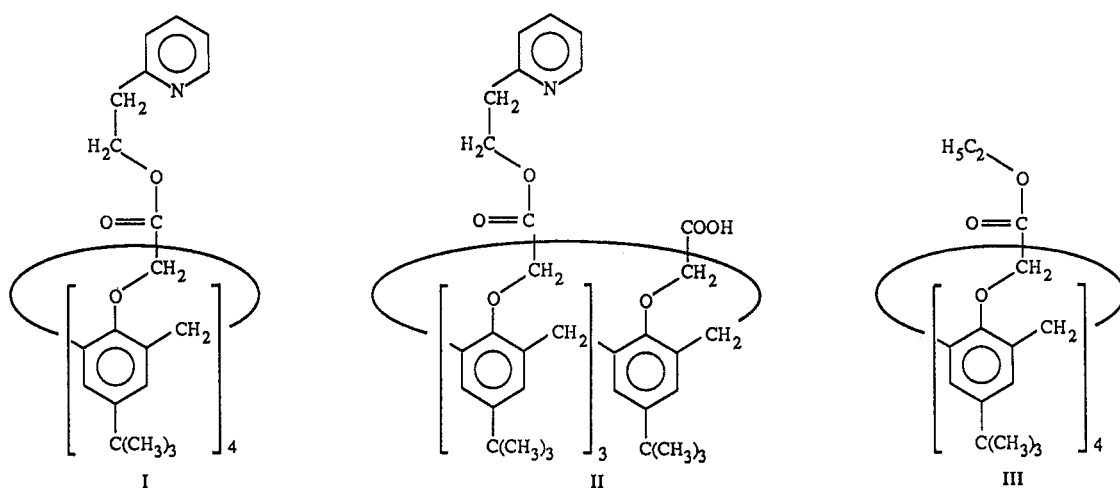
2.3. Phase transfer agents

The calixarene III was found to improve significantly the yield of product of the nucleophilic displacement of bromide in phenacyl bromide by acetate or by azide in acetonitrile (ref. 18).
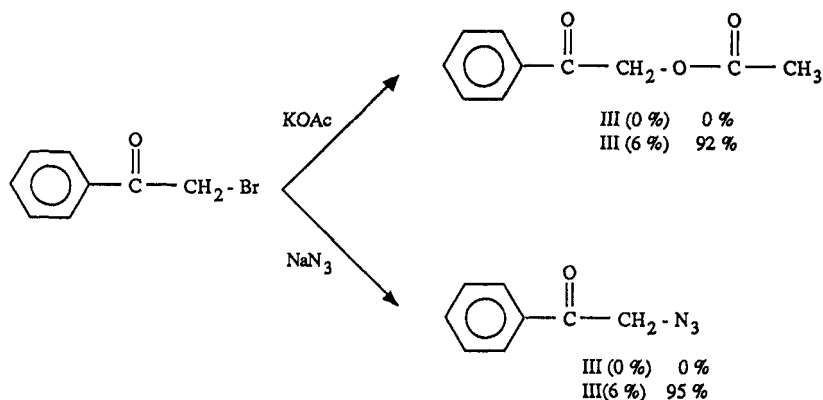
Fig. 8. Phase transfer catalysed reactions ; yield after 30 min heating in acetonitrile in the presence of 6 % III and in the absence of III.

Polyethyleneglycol modified calixarenes have been used as phase transfer agents for reaction in non polar media. The use of modified calix[6]arene IV as phase-transfer agent for the formation of ether through the Williamson synthesis has been reported to be more effective in comparison with oligoethyleneglycols or oligoethyleneglycol ethers (ref. 19).
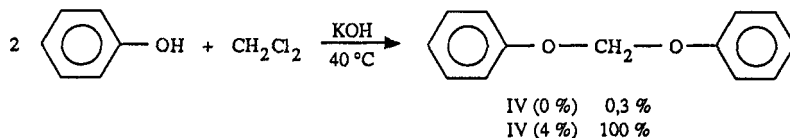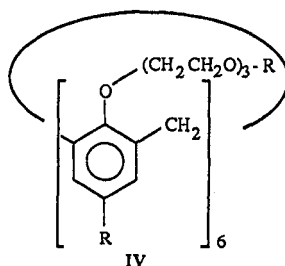

Fig. 9. Williamson ether synthesis catalyzed by IV ; yields after 24 h with and without catalyst.

2.4. Accelerators for instant adhesives

Several patents (ref. 20) claim the use of certain modified calixarenes as accelerants for cyanoacrylate instant adhesives. These additives render the adhesive capable of bonding porous substrates such as paper, leather, fabric and woods.

For example, when ethylcyanoacrylate, stabilized with 10 ppm BF_3 is used as the base adhesive formulation, Harris et al have shown that with the modified calix[4]arene V the fixture time on copy paper can be less than 1 s as against 60 s without additive.
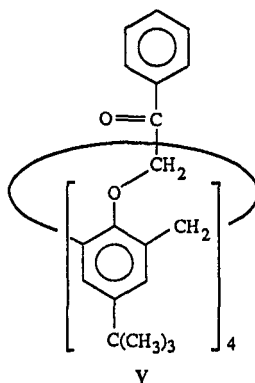
2.5. Ion scavengers for electronic devices

Ester and ketone modified calixarenes with alkali-metal sequestering properties are used as metal cation-immobilising additives for electronic encapsulants such as epoxides and silicones.

Harris et al (ref. 21) indicate that these modified calixarenes are at least as effective as crown ether in reducing levels of extractable ions. Typically extractable Na^+ levels can be reduced from 240 ppm to less than 30 ppm utilising 1-5 % by weight of a calixarene derivative in epoxide. Similar results were obtained with a wide range of alternatively modified calixarenes and oxacalixarenes.

2.6. Langmuir–Blodgett films and membranes

Monolayer films have been successfully made with several calixarenes. Bohmer et al (ref. 22), Shinkai et al (ref. 23) succeeded in making stable Langmuir monolayers from p-octadecyl-calix[4]arene or ester modified calixarenes.

Ultrathin monolayers and vesicles from calix[6]arenes were reported by Regen et al (ref. 24) ; these authors described "porous" monolayers made from novel mercurated calix[6]arenes VI which may be additionally stabilized by crosslinking with malonic acid.

VI
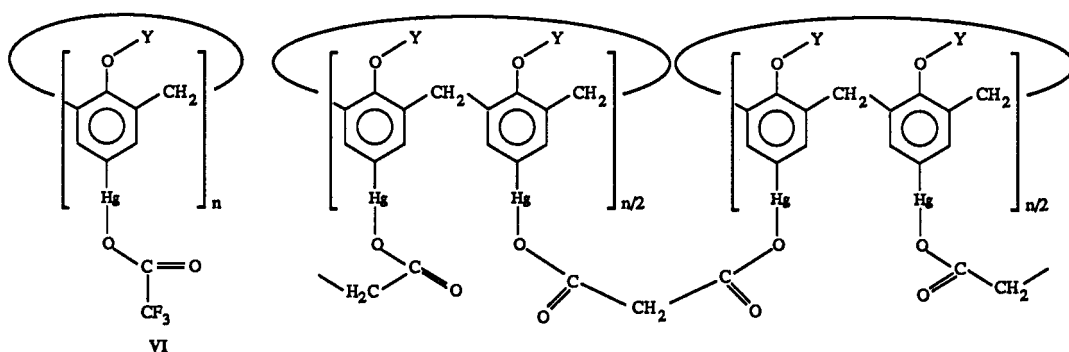
Very recently, hard and heat resistant film has been obtained with modified methylcalix[n]arenes (ref. 25). Methylcalixarenes are practically insoluble in all solvents. It has been discovered that acetylation of methylcalixarenes brings about surprising increases in solubilities in organic solvents and that unexpectedly, high heat resistance of methylcalixarene is not marred. The hexamer VII is particularly of interest because it exhibits the highest solubilities in various organic solvents. The heat-resistant film (up to 400 °C) can easily be removed either entirely or selectively, by using an organic solvent since the film-forming process does not include any chemical reaction of the calixarene VII.

VII
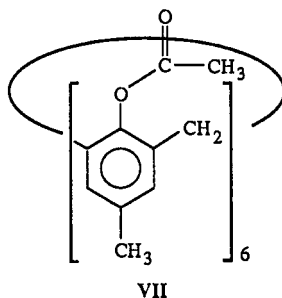
2.7. Catalytic properties

Several authors have shown the catalytic properties of modified calixarenes in hydrolysis reactions. For instance p-trimethylamino O-alkylcalix[4] and [6]arene salts VIII are used to catalyzed the base hydrolysis of p-nitrophenyl dodecanoate (ref. 26).

Recently Harris et al (ref. 27) have shown the catalytic properties of p-tert-butyl O-ethoxycalix[4] and [6]arene IX in a free radical polymerisation process. The calixarene acts as a complexing agent (table 5) in the polymerisation process of acrylic monomers using the metal salt as free radical initiator.
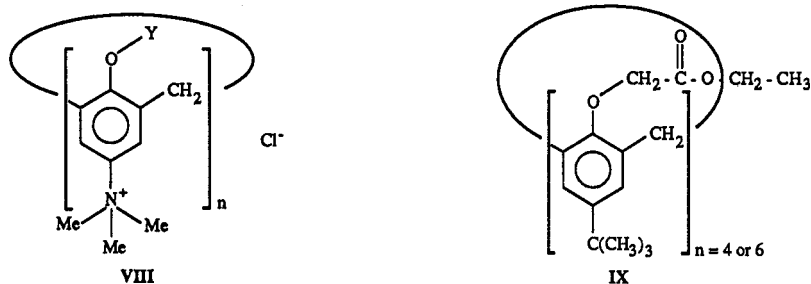

TABLE 5. Catalytic properties of IX in a free radical polymerisation process.

Complexing (agent)	Amount (mmol)	Reaction (time mn)	% Conversion to polymer
None	---	20	39
None	---	40	47
[IX] n = 4	0.09	20	92
[IX] n = 4	0.09	40	97
15-Crown-5	0.09	20	66
15-Crown-5	0.09	40	75

CONCLUSIONS

The results presented demonstrate the wide range of possible applications of calixarenes. Other applications have not been discussed here, for example polymer calixarenes, ion selective electrodes and field effect transistors which have been treated in the review (ref. 2). There are also calixarene deodorant compositions (ref. 28) electrostatographic toners (ref. 29) and azomethane-type liquid crystals (ref. 30). The patents which concern calixarene preparation have not been taken into account. They are also of importance as it is necessary to obtain sufficient quantities of the product in order to study the possible applications.

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