SUPRAMOLECULAR CHEMISTRY OF NITROGEN DIOXIDE

by

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ABSTRACT

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Supramolecular chemistry has been defined as “chemistry beyond molecules”, and involves investigating molecular systems held together reversibly by intermolecular forces, not by covalent bonds. This dissertation discusses a supramolecular approach towards sensing, entrapment and utilization of NO₂/N₂O₄ gases. Chapter 1 briefly discusses supramolecular chemistry and supramolecular chemistry of gases.

In chapter 2, the interaction of NOₓ with metalloporphyrins is described. Specifically, ruthenium nitrosyl derivatives hold a special place in mimicking bio-relevant NO–metal interactions. A previously unnoticed reaction between NO₂/N₂O₄
and a Ru(II) porphyrin is described. It causes disproportionation of N₂O₄ and leads to a stable nitrosyl nitrate complex. Our findings offer a new insight into the mechanism of sensing and fixation of NO₂/N₂O₄ by metalloporphyrins.

In chapter 3, the reaction between calixarenes and NO₂/N₂O₄ gases was investigated. Exposure of tetra-O-alkylated *cone* or *1,3-alternate* calix[4]arenes to NO₂/N₂O₄, both in chloroform solution and in the solid state, resulted in deeply colored calixarene-nitrosonium (NO⁺) complexes. In the presence of a Lewis acid, such as SnCl₄, stable calixarene-NO⁺ complexes were isolated in a quantitative yield and fully characterized. NO⁺ is found encapsulated within the calixarene cavity, and forms a stable charge-transfer complex. The NO⁺ encapsulation was also demonstrated in titration experiments with calixarenes and NO⁺SbF₆⁻ salt in chloroform. The complexation process is reversible, and the complexes dissociate upon addition of water and alcohol, recovering the parent calixarenes.

Chapter 4 describes the polymer supported calixarenes. Functionalized calix[4]arenes were synthesized and attached to silica gels and polyethyleneglycol (PEG), which afforded solid materials capable of visual detection and entrapment of NO₂/N₂O₄ both in the solid state and solution.

The concept of encapsulated nitrosating reagent was introduced in chapter 5. Stable calixarene-NO⁺ complexes act as encapsulated nitrosating reagents; cavity effects control their reactivity and selectivity. They were effectively used for nitrosation of secondary amides. Unique size-shape selectivity was observed, allowing for favorable nitrosation of only less crowded N-Me amides. For robust, silica gel and PEG
based calixarene materials, similar size-shape selectivity was observed. Enantiomerically pure encapsulating reagents were tested for nitrosation of racemic amide, showing modest but reproducible stereoselectivity.
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CHAPTER 1

INTRODUCTION

1.1 Supramolecular Chemistry of Gases

The importance of supramolecular chemistry was fully recognized when Donald J. Cram, Jean-Marie Lehn, and Charles J. Pedersen were jointly awarded the Nobel Prize for Chemistry in 1987 for their work on inter-molecular, host-guest complexes and assemblies of molecules.

Supramolecular chemistry focuses quite literally on going "beyond" molecular chemistry (Figure 1.1).\textsuperscript{1,2,3} It can be described as the study of systems which contain more than one molecule, and it aims at understanding the structure, function, and properties of these assemblies. A supramolecular assembly is a multi-component system
of atoms, ions, and/or molecules which are held together by non-covalent interactions such as hydrogen bonds, Van der Waals forces, π - π interactions, and/or electrostatic effects. The latter mode of bonding is particularly important for assemblies involving metal ions. These various bonding interactions are weaker than covalent bonding; therefore supramolecular assemblies are usually less stable than molecular compounds. For example, they can be easier to break apart at high temperatures or if they are mixed with acid.

One of the major goals of supramolecular chemists is the synthesis of supramolecular assemblies which have new functions that cannot arise from a single molecular species. These functions are based on novel mechanical properties, magnetic properties, light responsiveness, catalytic activity, fluorescence, redox properties, etc.

These new functions may lead to the application of these assemblies as switchable materials, high-tech sensors for pollutants in air or water, compact information storage devices for next-generation computers, as high-performance catalysts in industrial processes, as contrast agents for CAT or MRI scans, or as chemical reaction containers. Supramolecular chemistry is intimately related to nanotechnology, and many promising nanotech devices are based on the principles of supramolecular chemistry.

Gases occupy a central position in biomedicine, science, technology, and agriculture. The chemistry of gases dates back to the 18th century, when most of them were discovered and described. However, gases are technically more difficult to handle than liquids and solids. In addition, their molecules are neutral, and electrostatic binding
interactions are much less effective than they would be for similar-sized cations and anions, although a number of gas molecules have dipole or quadrupole moments.

The field of supramolecular chemistry of gases was reviewed by Dr. Rudkevich’s group.\textsuperscript{5} The gases that surround us are not ideal gases and they interact with other molecules, and thus their recognition/complexation is possible. Gases are small molecules with a size of 2-4 Å and very close contacts with supramolecular receptor sites are needed to achieve their binding.

Nature employs molecular recognition for effectively discriminating between blood gases, with differences in the O\textsubscript{2} / CO binding with heme molecules being the most spectacular example.\textsuperscript{6} In addition to the iron-gas interaction, the histidine residue on the distal porphyrin face of hemoglobin and myoglobin is involved in hydrogen bonding with O\textsubscript{2} (1, Scheme 1.1), as evident from EPR, X-ray, and neutron-diffraction studies. Such hydrogen-bonding interactions not only affect oxygen affinity, but may also stabilize the oxygen molecule and prevent autoxidation. The distal cavity is also important, particularly the polarity of the walls, the functional composition, and the 3D arrangement.

In oxygen-avid Ascaris hemoglobin, glutamine and tyrosine residues participate in hydrogen bonding with O\textsubscript{2} (2, Scheme 1.1).\textsuperscript{7} The crystal structure of complex 2 shows the tyrosine hydroxyl group to be perfectly positioned to make a strong hydrogen bond with the distal atom of the complexed O\textsubscript{2}, and the glutamine forms a somewhat weaker hydrogen bond to the oxygen atom coordinated to the iron center. There is also a hydrogen bond between the tyrosine and glutamine fragments. This hydrogen-bonding
network is believed to be responsible for the $K_d$ values for $O_2$ being four orders of magnitude greater than that of human hemoglobin.

Scheme 1.1 Molecular recognition of gases in Nature.

The crystal structures of complexes of heme protein with nitric oxide (NO) also suggest that the distal cavity is important in gas binding. Such cavities are rather hydrophobic and possibly help to exclude the noncoordinated $H_2O$ molecule prior to the
complexation of NO. The X-ray structure of the ferrous-nitric oxide complex of native sperm whale myoglobin 3 (Scheme 1.1) shows a FeNO interaction as well as the formation of a hydrogen bond between the gas molecule and the histidine 64 residue on the distal porphyrin face of the myoglobin. Overall, the NO binding event takes place in a tight cavity formed by the lipophilic leucine 69 and valine 68 fragments as well as histidine 64.

It is believed that upon atmospheric N₂ fixation by enzymes (such as Fe Mo nitrogenase), the NH nitrogen-metal intermediates 4 participate in hydrogen-bonding interactions with the amino acid residues of the enzyme (Scheme 1.1). These natural examples of supramolecular gas bonding assemblies offer great inspiration for designing of artificial receptors for gases. They directly point out the binding forces to employ and explore, in particular metal-gas interactions and cavity effects.

\[ R = (\text{CH}_2)_2\text{Ph} \]

Scheme 1.2 Encapsulation of CO₂ within hemicarcerand

\[ \text{CO}_2, \text{CDCl}_3 \]
Hemicarcerand (Scheme 1.2) - covalently sealed molecular containers with aromatic walls were first prepared by Cram et al. They encapsulate O\(_2\), N\(_2\), CO\(_2\), and Xe.\(^{10}\) The exchange between the free and bonded gas was slow on the NMR time-scale, with association constants (\(K_{\text{assoc}}\)) of 180 M\(^{-1}\) (N\(_2\)), 44 M\(^{-1}\) (O\(_2\)), and 200 M\(^{-1}\) (Xe) in CDCl\(_3\) at 22 °C, assuming a 1:1 stoichiometry. The volume of the inner cavity is relatively large (ca. 120 Å\(^3\)) compared to the gas molecules (ca. 40 Å\(^3\)). Hemicarcerands can probably accommodate more than one gas molecule, but this has not been investigated.

Metal - gas interactions were also studied. Dendritic porphyrins (Figure 1.2) bind O\(_2\) in preference to CO by a factor of >10. The porphyrin and its metal center provided a platform for the binding of O\(_2\). The unusually high O\(_2\) affinity was achieved presumably by hydrogen bonding between the bound gas and one of the NH residues of the amide moieties linking together the porphyrin core and the first-generation dendritic branches.

![Figure 1.2 Binding of O\(_2\) to a dendritic Fe(II) porphyrin.\(^{11,12}\)](image-url)

6
It is clear now, that Lewis acid-base, dipole-dipole interactions, hydrogen bonding, van der Waals forces, particularly constrictive encapsulation within enclosed spaces (cavities) and metal-gas interactions, and an intelligent combination of all these are most likely to work for gas recognition. The limited polarizability, dimensions, and geometries of the gas molecules necessitate a high degree of design and preorganization in the receptor to achieve complementarities, and often a combination of different binding forces is necessary.

1.2 Nitrogen Oxides

NO₂ is a reddish-brown, highly reactive gas that is formed by oxidation of NO in air at ambient temperature. NOₓ, the term used to describe the sum of NO, NO₂, N₂O₄ and other oxides of nitrogen, play a major role in the formation of ozone in the atmosphere through a complex series of reactions with VOCs (Volatile Organic Compounds).

Figure 1.3 Sources of NOₓ.
A variety of NO\textsubscript{x} compounds and their transformation products occur both naturally and as a result of human activities. Anthropogenic (i.e., manmade) NO\textsubscript{x} emissions account for a large majority of all NO\textsubscript{x} inputs to the environment. The major sources of anthropogenic NO\textsubscript{x} emissions are high-temperature combustion processes, such as those used in automobiles and fossil fuel burning power plants (Figure 1.3). Most NO\textsubscript{x} from combustion sources (~ 95\%) are emitted as NO; the remainder is largely NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4}. Because NO is readily converted to NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} in the environment, the emission estimates assume NO\textsubscript{x} are in the NO\textsubscript{2} form. Natural sources for the formation of NO\textsubscript{x} are lightning, biological and non biological processes in soil, and stratospheric intrusion. Ammonia and other nitrogen compounds, produced naturally, are important in the circulation of nitrogen through the ecosystem. Home heaters and gas stoves also produce substantial amounts of NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} in indoor settings.

![Figure 1.4 NO\textsubscript{x} emission trends.\textsuperscript{15}](image-url)
NO\textsubscript{x} gases are involved in the formation of ground-level ozone, participate in global warming, and also form toxic chemicals, nitrate particles and acid rain/aerosols.\textsuperscript{14, 16} NO\textsubscript{x} aggressively participate in various nitrosation processes in biological tissues.\textsuperscript{17} Free radical NO rapidly reacts with oxygen, producing N\textsubscript{2}O\textsubscript{3} (e.g., NO-NO\textsubscript{2}) and NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4}. These are powerful nitrosating agents, both in gas phase and in solution. The pathophysiological significance of NO\textsubscript{x} derives from their ability to generate mutagenic nitrosopeptides and further diazopeptides, to produce carcinogenic nitrosamines, and to nitrosate and further deaminate DNA nucleobases. For all these reasons, NO\textsubscript{x} emitting has been strictly controlled. According to The United States Environmental Protection Agency,\textsuperscript{14} national emissions of NO\textsubscript{x} have decreased over the past 20 years by more than 10\% (Figure 1.4) and the air quality has also improved (Figure 1.5). Tolerable levels of NO\textsubscript{x} are $\leq$ 5 ppm. Extensive NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} circulation in
the atmosphere requires not only its systematic monitoring but also necessitates the
development of improved methods of the NO₂/N₂O₄ fixation and utilization.

\[
\begin{align*}
\text{NO}_2 & \quad \text{N}_2\text{O}_4 \\
\text{N}_2\text{O}_4 & \quad \text{NO}^+\text{NO}_3^- \\
\end{align*}
\]

Figure 1.6 Structures of N₂O₄ (formal charges and electrons are omitted).

NO₂ is a paramagnetic gas since it has an unpaired electron on the nitrogen and
can dimerize to form N₂O₄.\textsuperscript{18,19} As the temperature rises, N₂O₄ rapidly dissociates back
to NO₂. Higher temperature and lower pressure favor NO₂, while lower temperature and
higher pressures favor N₂O₄. The position of the equilibrium between the two gases and
the color of the system vary with temperature. Below -21 °C, only pure, solid N₂O₄ is
present. Above 140 °C the system is 100% NO₂. At normal/standard conditions, the
dynamic interconversion between NO₂ and N₂O₄ makes it impossible to study either of
these species alone. N₂O₄ is known to exist in several isomeric forms, including
symmetrical O₂N-NO₂ and two \textit{cis-trans} ONONO₂ (Figure 1.6).\textsuperscript{20} The N-N bond in
N₂O₄ is quite weak. Of particular importance for us, N₂O₄ may disproportionate to ionic
NO⁻NO₃⁻ upon reacting with aromatic compounds (Figure 1.7).\textsuperscript{21}
\[
\begin{align*}
N_2O_4 & \rightleftharpoons 2NO_2 \\
N_2O_4 & \rightleftharpoons NO^+ + NO_3^-
\end{align*}
\]

Figure 1.7 NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} dissociation pathways.

Current NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} sensors are mostly electrochemical and monitor changes of potential or other electrical properties upon exposure of metal surfaces to these gases.\textsuperscript{22} In many cases however, other vapors - H\textsubscript{2}O, O\textsubscript{2}, HCl, HBr, SO\textsubscript{X}, and NH\textsubscript{3} can significantly influence the detection selectivity and therefore sensitivity. Optical sensors based on the coloration reaction between NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} and certain organic compounds are more selective as the reactions are specific. At the same time, the reuse of these sensors is not easy to achieve. To construct a reusable NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} specific chemical sensor, the reaction between NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} and sensing materials should be specific and reversible.

In the following chapters, the supramolecular chemistry of NO\textsubscript{x} is explored. The interactions of NO\textsubscript{x} and metalloporphyrins and calix[4]arenes are described.

1.3 Calix[4]arenes

Calixarenes are popular building blocks in molecular recognition.\textsuperscript{23} Considering the shape and size of calix[4]arenes, the sites of possible intermolecular forces and functional groups on them, their interaction with gases may lead to interesting results.

The name calix[n]arene was introduced in 1978 by Gutsche because of the vase (calyx) type structure.\textsuperscript{24} Calix[n]arenes are metacyclopahnes which are derived from the condensation of phenols and formaldehyde under different conditions.\textsuperscript{23,25} The ‘n’
stands for the number of aryl groups in the cyclic array. Although calixarenes have been known since the 1940’s, their structure was firmly established in the late 1970s, after which, they become the most popular molecules in supramolecular chemistry.

Calix[4]arenes have four conformations called cone (5), partial cone (6), 1,2-alternate (7), and 1,3-alternate (8, Figure 1.8) which differ in the relative orientation of the phenol rings.

![Figure 1.8 Conformations of calix[4]arenes.](image)

These conformations can be easily identified by unique sets of resonances in their $^1$H NMR and $^{13}$C NMR spectra. Particularly useful are the NMR patterns of the bridging methylene groups which are different for the various conformations (Figure 1.9). De Mendoza and coworkers have introduced a useful “rule” for correlating the conformation of calix[4]arenes and their NMR spectra.$^{26,27}$ By analyzing the peaks of the $^1$H NMR spectrum and / or $^{13}$C NMR spectrum, the calix[4]arene conformations can be determined (Figure 1.9).
For calix[4]arenes with the same substituents at each para position, an AX system is usually observed below the coalescence temperature for the methylene protons in the cone conformation, whereas a singlet is observed in the 1,3-alternate conformation. Both singlet and AB systems should be present in partial cone or in 1,2-alternate conformations, and the number and multiplicity of aromatic signals could be used to differentiate them. Since most calix[4]arenes interconvert above room temperature in a broad range of solvents, these observations are usually enough to assure the preferred conformations. However, such symmetry-controlled patterns are absent in stepwise assembled calix[4]arenes with different substituents at para-substituents or phenolic oxygen.

In the $^1$H NMR spectra, cone conformations have adjacent phenol rings in a syn orientation. Cone calix[4]arenes have two sets of doublets at ~3.1 ppm and 4.0 ppm. In 1,3-alternate conformations, adjacent phenol rings are in an anti orientation and result in
one peak at ~ 3.5 ppm. The presence of syn and anti phenol rings in partial cone and 1,2-alternate calix[4]arenes results three sets of signals at ~3.1, 3.5 and 4.0 ppm.

An inspection of the proton-decoupled $^{13}$C NMR spectra of calix[4]arenes revealed that the chemical shift of the methylene carbon appeared at ether 31 or 37 ppm. The former value was found in cone calix[4]-arenes. The latter was found for reported 1,3-alternate conformations. With slight distortions, two syn and two anti orientations are expected in the partial cone and 1,2-alternate calix[4]arenes. Consequently, two $^{13}$C NMR signals should be present for the methylene carbon atoms of calix[4]arenes in these conformations at 31 and 37 ppm.

Figure 1.10 C$_2$-C$_2$ interconversion of tetra alkoxy-calix[4]arene in the cone conformation.

Cone-shaped calix[4]arenes are ~ 4 Å deep and ~ 7 Å in diameter at the upper rim. Tetra-O-alkylated cone calix[4]arenes exist in the pinched C$_{2v}$ symmetrical conformation, with two opposite aromatic rings almost parallel and situated ~ 5 Å apart,
and two others flattened. This conformation is more preferable than the perfect cone $C_{4v}$ conformation because of the $\pi-\pi$ interaction between cofacial aromatic rings. The interconversion between two $C_{2v}$ structures is fast on the NMR time scale (Figure 1.10).$^{28}$

Because of two possible rotational modes of the phenol unit: the oxygen-through-the-annulus rotation and the $p$-substituent-through-the-annulus rotation, all four conformations of calix[4]arenes can interchange. The exchange however does not take place when the tetra-$O$-substituents are bulkier than $n$-Pr group.$^{29,30}$ Bulky groups can inhibit the oxygen-through-the-annulus rotation and, therefore, tetra-$O$-propylation results in conformationally immobile calix[4]arenes.

Calix[4]arenes in a 1,3-alternate conformation are much more rigid and possess a cylindrical inner tunnel, defined by two cofacial pairs of aromatic rings oriented orthogonal along the cavity axis. According to the number of X-ray studies, this tunnel is ~5-6 Å in diameter.$^{31}$

With a cavity composed of four electron rich aromatic ring and oxygen atoms, calix[4]arene can form good hosts for metal ions.$^{32,33}$ At the same time, modification of calix[4]arenes leads to anionic and neutral molecules receptors.

![Figure 1.11 Cone conformation of a calix[4]arene.](image-url)
Functionalization of calix[4]arenes is usually carried out at the upper rim and the lower rim (Figure 1.11). General approaches include alkylation, acylation, nitration, sulfon酰lation etc. Further functional group transformations by traditional methods afford other desired molecules. Tetraester calix[4]arene 9 is one of the best receptors for Na⁺ and calix[4] crown 10 selectively forms complex with Cs⁺ (Figure 1.12).³⁴ Anion³⁵,³⁶,³⁷ and neutral molecular²³c receptors based on calix[4]arenes have also been developed.

![Figure 1.12 Examples of metal cation receptors.](image)

When calix[4]arenes have chiral substituents, the cavity is also expected to have chiral properties. The shape of the cavity will determine the complexation properties of the hosts, therefore chiral calix[4]arenes would generate chiral environment in chiral encapsulation or recognition. These chiral complexes can be useful in organic synthesis (see Chapter 4).
1.4 Porphyrins

Porphyrrins are another class of molecular platforms widely used in supramolecular chemistry. They have been extensively explored by chemists because of the important role they play in the heme chemistry.\textsuperscript{38} Their coordination properties were studied with various gas species including oxygen (O\textsubscript{2}), carbon monoxide (CO) and NOx.\textsuperscript{38}

Metalloporphyrins of the Group 8 metals containing O-bound axial ligands are potential structural models for the heme-containing catalysts\textsuperscript{39} or the heme $d_1$ domain of cytochrome $cd_1$ nitrite reductase from Paracoccus denitrificans GB17 (Thiospaera pantotropha).\textsuperscript{40} These heme-containing biomolecules posses tyrosine as an axial ligand, and are known to react with nitric oxide (NO) to give heme-NO species. This helps to metabolize NO in living cells. Fe and Mn porphyrins complexes have been used mainly for catalytic oxidation reactions, and Zn and Rh, Co porphyrins have been used for chiral recognition.\textsuperscript{41} There has been a great deal of interest in Ru-porphyrin chemistry as viewed both in the complexation and catalytic contexts. The interest in Ru chemistry has been inspired by the periodic relationship of Ru to Fe and the possibility to prepare relatively stable oxo-Ru derivatives. Ru porphyrins are diamagnetic so NMR studies become easy.
CHAPTER 2
METALLOPORPHYRINS AND THEIR COMPLEXES WITH NOₓ

Supramolecular chemistry of porphyrins and NOₓ is important in understanding the NO metabolism in living system. In early reports, reactions between metalloporphyrins and NO₂ gas have been investigated; however, the mechanism was not so clear. Here, interactions between metalloporphyrins and NO₂/N₂O₄ are studied. Their utility in sensing of NO₂/N₂O₄ gas is described, and the chemistry occurring is discussed.

2.1 Introduction

Figure 2.1 Structure of porphyrin and heme.

Porphyrlins occur widely in nature, and they play very important roles in various biological processes. The basic structure of porphyrin 11 consists of four pyrrole units linked by four methine bridges (Figure 2.1). Heme (12) is the iron(II) protoporphyrin-
IX complex shown in Figure 2.1. It is the prosthetic group in hemoglobins and myoglobins, which are responsible for oxygen transport and storage in living tissues. Heme can also be found in the enzyme peroxidase, which catalyzes the oxidation of substrates with hydrogen peroxide. The related enzyme, also containing heme, accelerates the breakdown of hydrogen peroxide to water and oxygen. Other heme-containing proteins include the cytochromes, which serve as one-electron carriers in the electron transport chain. Because of the heme models, porphyrins are very important and widely studied.

The porphyrin macrocycle is an aromatic system containing 22 $\pi$ electrons, but only 18 of them are involved in delocalization. It obeys Hückel's rule of aromaticity ($4n + 2 \pi$ electrons where $n = 4$) and has been shown by X-ray crystallography to be planar. The aromatic character of porphyrins can also be seen by NMR spectroscopy. Due to the anisotropic effect from the porphyrin ring current, the NMR signals for the deshielded meso protons (protons on the bridging methine carbons) show up at low field (8 ~ 10 ppm), whereas the signals for the shielded protons on the inner nitrogen atoms show up at very high field (~ -2 to - 4 ppm).

In the absorption spectrum, the highly conjugated porphyrin macrocycle shows an intense absorption ($\varepsilon > 200000$) at $\lambda_{\text{max}} \sim 400$ nm (the Soret band), followed by several weaker absorptions (Q-Bands) at higher wavelengths ($\lambda_{\text{max}} = 450 - 700$ nm) (Figure 2.2). Variations of the peripheral substituents on the porphyrin ring often cause changes to the intensity and wavelength of these absorptions. Protonation of two of the inner nitrogen atoms or insertion of a metal into the porphyrin cavity also changes the
visible absorption spectrum. These absorptions can often be very helpful in studying intra- and inter-molecular interactions of porphyrins.

Figure 2.2 Typical UV-visible absorption spectrum of a porphyrin.44

The porphyrin ring is very stable to concentrated acids (e.g. sulfuric acid), and itself can act both as an acid and a base. Strong bases such as alkoxides can remove the two protons (pK_a ~16) on the inner nitrogen atoms of a porphyrin to form a dianion. On the other hand, the two free pyrrolenine nitrogen atoms (pK_a ~ 5) can be protonated easily with acids such as trifluoroacetic acid. The protonation - deprotonation process is generally accompanied by the absorption band changes and also results in a color change. These changes can be useful in construction of optical sensors for the reactive gases such as NO_2/N_2O_4, O_2, SO_2, HCl, H_2S etc.22b, 23e,45

Porphyrins undergo a number of chemical reactions typical for aromatic compounds. For example, electrophilic substitution reactions are often performed on the methine (meso) carbons and the β-pyrrolic carbons. Furthermore, certain substituents on
a porphyrin molecule can be modified. This leads to the availability of a variety of differently substituted porphyrins.

Another important feature of porphyrins is their ability to form metalloporphyrins. A number of metal ions (e.g. Fe, Zn, Cu, Ni, Co, Ru) can be readily inserted into the porphyrin cavity by using various metal salts (Figure 2.3). Removal of the metal can usually be achieved by treatment with strong acids or cyanides.

![Figure 2.3 Metalloporphyrin: M = Fe, Zn, Ru etc. L1, L2 are ligands. L = amines, OH, SR, O2 etc.](image)

Porphyrs and metalloporphyrins can form supramolecular complexes. The conjugated π-system of the macrocycle, the metal atom at the metalloporphyrin core and heteroatoms in the peripheral substituents play important role in the complexation processes. 46

2.2 Reactions of NO₂/N₂O₄ with Porphyrins

The interaction of metalloporphyrins with various NOₓ species is of enormous physiological importance. 47 Nitrosyl, nitrite, and nitrate metalloporphyrin complexes are involved in key processes in both the nitrogen cycle 48 and mammalian physiology, with examples of the latter including neurotransmission, vasodilation, and platelet
aggregation. A large number of iron heme complexes with NO have been obtained and characterized. Stable nitrosyl porphyrin complexes can be prepared by replacing iron with other transition metals, and Ru nitrosyl derivatives have been widely used in mimicking biorelevant NO-metal interactions.

In contrast to NO, chemistry between NO₂/N₂O₄ and metalloporphyrins is much less developed, probably due to the complexity of the reactions. We report here a previously unknown reaction between NO₂/N₂O₄ and a Ru(II) porphyrin. It causes disproportionation of N₂O₄ and leads to a stable nitrosyl nitrato complex. Our findings may offer a new insight into the mechanism of sensing and fixation of NO₂/N₂O₄.

We found that reaction of two equivalents NO₂/N₂O₄ with Ru(II) carbonyl tetra-p-tolylporphyrin Ru(TTP)(CO) in CH₂Cl₂ results in a rapid formation of nitrosyl nitrato Ru(TTP)(NO)(ONO₂) in 95% yield (Scheme 2.1).

Metals react with N₂O₄ with the formation of ionic NO⁺ NO₃⁻, and we propose, that the N₂O₄ disproportionation takes place for the described experiments here. NO⁺ then replaces the carbonyl, and nitrate coordinates at the other side of the porphyrin.

Scheme 2.1 Preparation of nitrosyl nitrato TTP: a) Ru₃(CO)₁₂, decalin, 190 °C, 12 h, 95%. b) NO₂/N₂O₄/CH₂Cl₂ 25 °C or NO₂/N₂O₄ gas.
Preparatively, 14 was synthesized from meso-tetratolyl porphyrin (TTP) in the presence of tris-Ru dodecacarbonyl (Ru₃(CO)₁₂) in decalin at 190 °C overnight. The orange solution of 14 turned dark-green upon addition of NO₂/N₂O₄. In the IR spectrum of 15 (in KBr), the carbonyl CO band of 14 at ν = 1950 cm⁻¹ is replaced by a new, very strong nitrosyl band NO at ν = 1852 cm⁻¹, characteristic for the linear Ru-NO geometry (Figure 2.4 A). In addition, nitrate bands appeared at ν = 1515, 1269, and 950 cm⁻¹. Reaction with NO₂/N₂O₄ caused obvious changes in the UV-vis absorption spectra of the porphyrin. Upon mixing, the Soret band at λᵥₘₓ = 412 nm decreased in its intensity, while the Q-band at λᵥₘₓ = 528 nm disappeared and a new band at λᵥₘₓ = 564 nm emerged (Figure 2.4 B). When the reaction was performed in an NMR tube in CDCl₃, the experiment resulted in a visible transformation of the spectra (Figure 2.4 C). In particular, prior to the NO₂/N₂O₄ exposure, the pyrrole -CH and the meso-tolyl CH protons of 14 were seen as a singlet at 8.70 ppm and two pairs of doublets (J = 7.5 Hz) at 8.08, 8.02, 7.52, and 7.50 ppm, respectively. After the reaction, these were transformed into a singlet at 9.08 ppm and three apparent doublets (J = 8.0 Hz) at 8.16, 8.14, and 7.61 ppm, 1:1:2 ratios, respectively.

For a spectroscopic comparison, Ru(TTP)(CO) 14 was treated with NO gas in CH₂Cl₂ (Scheme 2.2). As expected, nitrosyl nitrito Ru(TTP)(NO)(ONO) porphyrin 16 was obtained, whose features are different from those of 15. Specifically, in the IR spectrum of 16 (in KBr), a strong nitrosyl band NO at ν = 1842 cm⁻¹ and two nitrite bands were detected at 1512 and ν = 928 cm⁻¹. In the ¹H NMR spectrum of 16 in CDCl₃,
the pyrrole -CH are seen as a singlet at 9.01 ppm, and the meso-tolyl CH protons appear as two pair of doublets at 8.16, 8.08, 7.59, and 7.57 ppm.

Figure 2.4 Spectra of Ru(TTP)(NO)(ONO2) (15). A: FTIR spectrum of 15 in KBr. B: UV-vis spectral changes of Ru(TTP)(CO) (14) upon reaction with NO2/N2O4 in CH2Cl2. C: 1H NMR spectrum (500 MHz, CDCl3, 295 K) of 15 obtained from Ru(TTP)(CO) 14 and NO2/ N2O4. D: 1H NMR spectrum of 15 obtained from Ru(TTP)(NO)Cl 17 and AgNO3. The residual CHCl3 signal is marked “·.”
Independent structural evidence for complex 15 was obtained from the reaction of porphyrin Ru(TTP)(NO)Cl (17) with AgNO₃ (Scheme 2.3), following the procedure of Bohle and co-workers.⁵⁴ Treatment of a benzene-MeCN solution of 14 with AgNO₃ at room temperature resulted in a quantitative formation of the product, which possesses identical spectroscopic features with 15 (for example, Figure 2.4 D). Ru(TTP)(NO)(ONO) porphyrin 16 can be obtained analogously from 17 and AgNO₂ (Scheme 2.3).

Chemically, Ru(TTP)(NO)(ONO₂) 15 is quite stable and can be stored for weeks without protection at room temperature. This is in contrast to recently described Fe(III)(TPP)(NO)(ONO₂) complex,⁵⁶ which exists only at very low temperatures. At the same time, 15 essentially decomposes on silica gel, neutral and basic aluminum oxide.
columns, which indicates that the nitrate anion is rather weakly coordinated and can be lost or replaced upon chromatography.

Introducing higher concentrations of NO₂/ N₂O₄ leads to further transformations of 15. In the UV-vis spectra, second set of isosbestic points appears, with the broad shoulder growing at \( \lambda_{\text{max}} = 440 \) nm. In the \(^1H\) NMR spectra, the signals of 15 disappear and new sets emerge, featuring multiplets between 9.4 and 9.2 ppm. Most probably, nitration of the pyrrole rings occurs, as N₂O₄ has previously been used to nitrate metalloporphyrins into the \( \beta \)-position.₅⁷

### 2.3 Conclusions

In summary, a new reaction can now be added to the broad spectrum of processes between NOₓ gases and metalloporphyrins. NO₂/N₂O₄ rapidly disproportionates over a Ru(II) porphyrin with the formation of a Ru(II) nitrosyl nitrato complex. This and recently described Fe(III)(TPP)(NO)(ONO₂) are the only known nitrosyl nitrato metalloporphyrins, and in general, metalloporphyrin-nitrato adducts are rare. Notably, ambient temperature solution studies shows Fe(III)(TPP)(NO)(ONO₂) is unstable and easily decays to other products. This behavior is in contrast to the greater stability of the analogous Ru complex Ru(TTP)(ONO₂)(NO) which can now be prepared by the reaction of Ru(TTP)(CO) with NO₂/N₂O₄. While previously overlooked, these complexes may be very important intermediates in biological and industrial processes involving NOₓ and porphyrins. For instance, Ford group has used our data to explain the pathway of forming Fe(TPP)(NO₂)(NO) during reaction of Fe(TPP)(ONO₂)(NO) with NO. Furthermore, while metalloporphyrin and
phthalocyanines have been known for years as effective sensors for NO$_2$/N$_2$O$_4$, the chemical reactions and structures responsible for this are still largely unknown. Our findings provide insight into the mechanism of NO$_2$/N$_2$O$_4$ sensing by metalloporphyrin.

In the meantime we noticed that rapid, orange-to-green color changes upon exposure of porphyrin 14 to NO$_2$/N$_2$O$_4$, both in solution and in the thin film, could be conveniently utilized for the gas sensing. Optical sensors based on this coloration reaction can be developed.
CHAPTER 3
SUPRAMOLECULAR INTERACTIONS BETWEEN CALIX[4]ARENES AND NO$_2$/N$_2$O$_4$

3.1 Properties of Cone and 1,3-alternate Calix[4]arenes

Complexes of calix[4]arenes with neutral molecules are weak. The cavities are obviously too small and they also lack additional binding sites. In most of the X-ray structures of the inclusion complexes of calix[4]arenes, the guest molecule is positioned not inside but roughly above the plane defined by the upper carbon atoms of the cyclic polyaromatic skeleton. On the other hand, cations are known to more strongly interact with the calixarene π-surface. Ammonium ions and metal cations were found complexed within the cone-shaped cavities. 1,3-Alternates, functionalized with appropriate binding sites on the phenol oxygen, bind metal cations - Na$^+$, K$^+$, and Ag$^+$ - both with "hard" oxygens and "soft" π-basic aromatic rings.

Recently, Kochi, Rathore and co-workers described very stable complexes between calix[4]arenes and NO$^+$ cation, both in solution and in the solid state. The NO$^+$ cation was found encapsulated within the calix[4]arene cavity (Figure 3.1 X-ray analysis), and strong charge-transfer interactions with the π-surface of calix[4]arene positioned the guest between the cofacial aromatic rings at a distance 2.4 Å, which is much shorter than the typical Van der Waals contact (3.2 Å).
Based on the above precedent, it is expected that interactions between NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} and calix[4]arenes might lead to disproportionation of NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4} and formation of calix[4]arene - NO\textsuperscript{+} complexes. Below, a sequence of experiments elaborating this idea is described.\textsuperscript{62}

### 3.2 Synthesis of Calix[4]arenes

The synthesis starts from the commercially available tetra-tert-butyl calix[4]arene. Calix[4]arenes 18 and 21, possessing a cone and a 1,3-\textit{alternate} conformation, respectively, were synthesized through \textit{O}-alkylation of the corresponding parent calix[4]arenes with \textit{n}-hexylbromide (Scheme 3.1). In the synthesis of 18, NaH was employed as a base in hot DMF.\textsuperscript{63} Preparation of 21 includes the two-step alkylation of de-\textit{tert}-butylated calix[4]arene with \textit{n}-hexylbromide, using successively K\textsubscript{2}CO\textsubscript{3} and then Cs\textsubscript{2}CO\textsubscript{3} to reverse the conformation to 1,3-\textit{alternate} in boiling MeCN.\textsuperscript{64}
Bromination of 21 with NBS in acetone afforded tetrabromocalix[4]arene 22 in 53% yield (Scheme 2.2). Tetrahydroxylated 1,3-alternate derivative 23 was obtained through bromine-lithium exchange\(^{65}\) in 22 (n-BuLi, THF, -78 °C), followed by treatment with B(OMe)\(_3\) and oxidation with H\(_2\)O\(_2\) and aqueous NaOH (40% yield for three steps). Calix[4]arene 23 was subsequently alkylated with \(n\)-hexylbromide and NaH in hot DMF to yield octa(hexyloxy)calix[4]arene 24 in 85% yield.\(^{62}\)
Scheme 3.2 Synthesis of octasubstituted 1,3-alternate calix[4]arenes. (a) NBS, acetone, rt, 48 H, 53% yield. (b) n-BuLi (60 eq), THF, -78 °C, 0.5 h. (c) B(OMe)₃, -78 °C to 0 °C. (d) H₂O₂, aq NaOH, -78 °C to 25 °C, 40%, three Steps). (e) n-hexyl bromide, NaH, DMF, 70 °C, 24 H, 85%.

Using the similar procedures, 1,3-alternate tetra t-butyl calix[4]arene 27 and 28 were synthesized using successively K₂CO₃ and then Cs₂CO₃ (Scheme 3.3).

Scheme 3.3 Synthesis of 1,3-alternate calix[4]arene 27 and 28. (a) n- hexyl bromide/n- propyl bromide, K₂CO₃, MeCN, 80 °C, 48 h, 76% / 81%. (b) n-hexyl bromide/n- propyl bromide, Cs₂CO₃, MeCN, 80 °C, 48 h, 42% / 49%.

3.3 Complexation Studies with NO₂/N₂O₄

Bubbling NO₂/N₂O₄ through the solutions of 18, 21, 24, 27 and 28 in CHCl₃ (Scheme 3.4, Scheme 3.5) instantly results in a deep colored solution. Solutions of 18, 24, 27 and 28 turned dark blue, and solution of 21 became deep purple. The UV-vis
absorption spectra changed accordingly: broad bands appeared at $\lambda_{\text{max}} = 560, 512, 600$ and $578, 565$ nm for NO$_2$/N$_2$O$_4$ exposed solutions of 18, 21, 24, 27 and 28 respectively. This is in a striking contrast to colorless solutions of 18, 21, 24, 27, 28, and pale yellow solution of NO$_2$/N$_2$O$_4$ in CHCl$_3$, and implies a charge-transfer process has occurred.

This process was difficult to monitor. Interaction of NO$_2$/N$_2$O$_4$ with 18, 21, 27 and 28 is very dynamic, and the initial $^1$H NMR analysis of the solutions gave rather complex, quickly changing spectra. The NO$_2$/N$_2$O$_4$ mixture is known as an effective nitrosating/nitrating agent. Not surprisingly, the NO$_2$/N$_2$O$_4$-containing CHCl$_3$ solutions of 18, 21, 27 and 28 bleached within 1-2 h, yielding mixtures of known $p$-nitrated calix[4]arenes (Scheme 3.4, Scheme 3.5, preparative TLC, $^1$H NMR).$^{30, 32, 36, 66}$
Scheme 3.5 Reactions between NO$_2$/N$_2$O$_4$ and calix[4]arene $27, 28$.

At the same time, when treated with SnCl$_4$, solutions of $18, 21, 27$, and $28$ and 2-3 equivalents of NO$_2$/N$_2$O$_4$ did not yield the nitration products. It is known that Lewis acids stabilize arene - NO$^+$ charge-transfer complexes.$^{21}$ Precipitation with hexanes resulted in deeply colored, moisture sensitive solids, assigned to NO$^+$ complexes $29, 31, 35$, and $36$ (>90% yield, Figures 3.3 - 3.4). These complexes are very stable and can be stored, in the absence of moisture, for several weeks, both in CHCl$_3$ solution and in the solid state. Complexes $29, 35$, and $36$ are dark blue, and complex $31$ is deep purple.

We proposed that these are encapsulation complexes with NO$^+$ deeply entrapped inside the π–electron rich calix[4]arene tunnel.

To demonstrate complex formation, an alternate route was adopted using an NO$^+$ salt to react with calix[4]arenes. Independent structural evidence came from the complexation experiments between calix[4]arenes $18, 21$ (Figure 3.2, Figure 3.3) and $24$ and commercially available NO$^+$/SbF$_6^-$ salt. Specifically, the CDCl$_3$ solutions of $18$...
and 21 were treated with NO\(^+\)SbF\(_6\)^{−} at 295 K and the complexation induced changes in the UV-vis, FTIR, and \(^1\)H NMR spectra were recorded. Under these conditions, the complexation process proved to be rather slow, however after ~20 h no starting calix[4]arenes 18, 21 were observed and the corresponding UV-vis, FTIR, and \(^1\)H NMR spectra exhibited features similar to those of NO\(^+\) complexes 29 and 31. These spectral data are in agreement with Kochi and Rathore’s spectral observations (see page 28-29). These experiments demonstrate that NO\(_2\)/N\(_2\)O\(_4\) disproportionates in the presence of calix[4]arenes and help generating NO\(^+\) species.
The association constants for the complexes were too high to be measured by the $^1$H NMR technique. Even slight excess of NO$^+$SbF$_6^-$ results in the complete complex formation in CDCl$_3$, and no free calix[4]arenes 18 and 21 were observed after equilibration. $K_{assoc}$ values $>10^6$ M$^{-1}$ ($\Delta G^{295} > 8$ kcal mol$^{-1}$) were estimated for the complexes, which is in agreement with the published values in CH$_2$Cl$_2$.\textsuperscript{67} Although complexes 18·NO$^+$SbF$_6^-$ and 21·NO$^+$SbF$_6^-$ formed slowly, it took only few minutes to form a complex with more electron rich calix[4]arene 24. Moreover, electrophilic NO$^+$ tends to further react with 24·NO$^+$SbF$_6^-$, and unidentified impurities were seen in the NMR spectrum already after several minutes. Unlike complexes 18·NO$^+$SbF$_6^-$ and
\(21\cdot\text{NO}^+\text{SbF}_6^-\), which are chemically stable for weeks, complex \(24\cdot\text{NO}^+\text{SbF}_6^-\) decomposes within a day (\(^1\text{H NMR})^67\).

**1,3-alternate** calix[4]arenes 27 and 28 also react with \(\text{NO}_2/\text{N}_2\text{O}_4\) to form similar complexes 35 and 36. Their NMR spectra have similar changes in patterns as 29 and 31. Complex 27:NO⁺SbF₆⁻ and 28:NO⁺SbF₆⁻ were also prepared using NO⁺SbF₆⁻ salt. In the presence of SnCl₄, 27, 28 reacted with \(\text{NO}_2/\text{N}_2\text{O}_4\) forming stable NO⁺ complexes.

### 3.3.1 Evidence of NO⁺ Encapsulation in Calix[4]arenes

We have mentioned that in the calix[4]arene - NO⁺ complexes, NO⁺ was entrapped deep in the cavity of calix[4]arenes. Similar encapsulation of NO⁺ into the cavity of calix[4]arenes was discussed by Kochi et al., whose crystal structure of a complex proved that NO⁺ was deep in the cavity.\(^67\) Despite the fact that our complexes were generated from \(\text{NO}_2/\text{N}_2\text{O}_4\) and calixarenes, and Kochi’s complexes were obtained from NO⁺ and calix[4]arenes or NO gas and calixarene radical cation, analogous spectra were recorded.

The encapsulation was further confirmed in experiments with anisoles (e.g., methoxybenzene). Only pale coloration was observed upon its exposure to \(\text{NO}_2/\text{N}_2\text{O}_4\).

Further more, when a sterically blocked calix[4]arene was tested, no coloration or complex formation were observed. Mesitylene derived 1,3-\textit{alternate} calix[4]arene 34 was obtained for comparison, according to the literature procedure by Pappalardo\(^68,69\) and subsequent \(O\)-alkylation with \(n\)-hexylbromide (Scheme 3.6). In this case, with a sterically \textit{blocked} and conformationally much more \textit{rigid} cavity, no coloration of 34 was observed. In 34, the pair of methyl groups in the \textit{ortho}-positions to the oxygen
forces the methyl groups of the adjacent aromatic rings toward each other, not only blocking an access to the cylindrical inner cavity, but also significantly rigidifying it. The same effect takes place on the other side of the calix[4]arene 34, which makes its interior completely hindered. Accordingly, NO\(^+\) guests can not enter the cavity.

![Scheme 3.6 Preparation of Pappalardo’s calixarene.](image)

Scheme 3.6 Preparation of Pappalardo’s calixarene. a) \(n\)-hexyl bromide, NaH, DMF, 70 °C, 72 h, 50%.

![Figure 3.4 NO\(^+\) complexation with Pappalardo’s calixarene.](image)

Figure 3.4 NO\(^+\) complexation with Pappalardo’s calixarene.

O-methylated calix[5]arene, calix[6]arene and calix[8]arenes did not react with \(\text{NO}_2/\text{N}_2\text{O}_4\) and \(\text{NO}^+\text{SbF}_6^-\). These model experiments emphasize the importance of
preorganized calix[4]arene cavities in the described transformations and confirmed that the NO\(^+\) is coordinated inside 18, 21, 27 and 28 (Figure 3.2, Figure 3.3).

3.3.2 UV-vis Absorption Studies

The UV-vis spectrum of calix[4]arene titration showed broad charge-transfer bands at \(\lambda_{\text{max}}\sim 560-580\) nm (\(\varepsilon = 8\times10^3\) M\(^{-1}\) cm\(^{-1}\)) (Figure 3.5), which is characteristic for arene-NO\(^+\) complexes.\(^{71}\) While neither calix[4]arenes nor NO\(_2\)/N\(_2\)O\(_4\) absorb in this region, addition of as little as \(~ 1\) equiv NO\(_2\) (\(~ 6\times10^{-5}\) M in CH\(_2\)Cl\(_2\)) to the solution of NO\(_2\) (\(6\times10^{-5}\) M in CH\(_2\)Cl\(_2\)) results in appearance of the charge-transfer band. Its absorbance grows upon addition of larger quantities of NO\(_2\)/N\(_2\)O\(_4\) and reaches saturation when \(~ 10\) equiv NO\(_2\) (e.g., 5 equiv N\(_2\)O\(_4\)) is added. From the titration
experiments, the apparent $K_{\text{assoc}}$ value was estimated to be $\sim 10^4 \text{M}^{-1}$. Accordingly, calix[4]arenes can detect NO$_2$/N$_2$O$_4$ at micromolar concentrations.

### 3.3.3 NMR Spectral Studies of Calix[4]arene - NO$^+$ Complexes

The $^1$H NMR spectra of 29 and 31 exhibited new sets of the calix[4]arene signals (Figure 3.6). In particular, aromatic CH protons of guest-free 18 were seen as a singlet at 6.76 ppm. In NO$^+$ complex 29, these were transformed into a singlet at 6.99 ppm. The methylene bridge CH$_2$ protons of 18 were recorded as doublets at 4.41 and 3.12 ppm ($J = 12.5$ Hz). In complex 29, these were seen as doublets at 4.39 and 3.44 ppm ($J = 13.0$ Hz). The aromatic protons of free 21 were seen as a doublet and a triplet, 2:1, at 6.92 and 6.68 ppm, respectively ($J = 7.5$ Hz). In NO$^+$ complex 31, these were transformed into a triplet and a doublet, 1:2, at 7.17 and 7.08 ppm, respectively ($J = 7.5$ Hz). The methylene bridge CH$_2$ and OCH$_2$ protons of 21 were seen as a singlet and a triplet, 1:1, at 3.62 and 3.54 ($J = 7.5$ Hz), respectively. In complex 31, these were transformed into a singlet and a triplet, 1:1, at 3.60 and 3.87 ($J = 7.5$ Hz), respectively.

The FTIR spectra exhibited characteristic arene - NO$^+$ stretching for example at $\nu = 1923$ and 1955 cm$^{-1}$ for 29 and 31, respectively.$^{21}$ Elemental analysis of extremely moisture sensitive and thermally unstable 29 and 31 proved to be difficult but reproducibly showed the CHN ratios corresponding to the presence of only one NO$^+$ cation in both structures. Similar spectral characteristics were observed for calix[4]arenes 24, 27 and 28. Calix[4]arenes complexes 35, 36 with $t$-butyl groups have similar NMR pattern besides the $t$-butyl group around 1.0 ppm. They are also moisture sensitive.
Figure 3.6 Portions of the $^1$H NMR spectra (500 MHz, CDCl$_3$, 295 ± 1 K).
(a) Calix[4]arene 18. (b) NO$^+$ complex 29; the identical spectrum was obtained upon addition of NO$^+$SbF$_6^-$ to 18. (c) Calix[4]arene 21. (d) NO$^+$ complex 31; the identical spectrum was obtained upon addition of NO$^+$SbF$_6^-$ to 21. The residual CHCl$_3$ signals are marked "·" (R = C$_6$H$_{13}$).
Addition of H₂O or MeOH to the freshly prepared CHCl₃ solutions of 29, 31, 35, 36, and the NO⁺ complexes prepared from 18, 21, 27 and 28 and NO⁺SbF₆⁻, resulted in complete complex dissociation and recovery of calix[4]arenes 18, 21, 27 and 28 (> 95% preparative TLC, UV-vis, ¹H NMR).

3.4 Dynamics of Calix[4]arene - NO⁺ Complexes

As evident from the ¹H NMR data, the NO⁺ exchange in and out of the cavity is slow on the NMR time scale. For example, in the titration experiments between calix[4]arenes 18, 21 and 28 and NO⁺SbF₆⁻, both free and complexed species can be observed separately. This is typical for the host-guest complexes with high $K_{assoc} > 10^6$ M⁻¹ values. On the other hand, the NO⁺ guest, with a van der Waals dimension <2 Å, freely migrates within the cavity at room temperatures (Figure 3.7). Indeed, the ¹H NMR spectra of complexes 29, 31 and 36 possess the same symmetry as guest-free calix[4]arenes 18, 21, 28 which in principle should be reduced upon complexation with nonsymmetrical NO⁺.

Cone calix[4]arene complex 29 should have a pinched, $C_{2v}$ symmetrical conformation, since only two opposite, co-facial aromatic rings trap NO⁺. Instead, the observed at room-temperature NMR spectrum exhibits a $C_{4v}$ symmetry, indicating a fast, on the NMR time scale, exchange between two $C_{2v}$ structures. 1,3-Alternate calix[4]arene complexes 31 and 36 should exhibit $C_{2v}$ symmetry, with two different top and bottom halves of the skeleton. Instead, the apparent at room-temperature symmetry is $S_4$, with equal top and bottom halves.
At the same time, the complexation process is reversible, and the NO$^+$ guest can still leave the calix[4]arene cavity. Addition of H$_2$O to the freshly prepared CHCl$_3$ solutions of 29, 31 and 36 resulted in the complete dissociation and recovery of calix[4]arenes 18, 21, 28. Interestingly, complex 31 bleached within seconds, but it took several minutes for con $t$-butyl calixarene complex to decompose. We propose that the kinetics of the process are responsible. Apparently, the $t$-Bu groups at the upper rim of the latter complex pose a significant steric hindrance and protect the encapsulated NO$^+$ species from the entering H$_2$O. Such stability of the arene-NO$^+$ complexes is without precedent.$^{71}$

On the other hand, NO$^+$ guest can be transferred from one calix[4]arene container to another (Figure 3.8). Calix[4]arene 24 was specifically designed to promote such transfer from the preformed complex 31. Four additional, electron donating
O(CH₂)₅CH₃ groups were introduced in the p-positions to the initial set of O(CH₂)₅CH₃ groups. This makes the cavity in 24 significantly more π-electron rich and dramatically increases its affinity toward positively charged NO⁺. At the same time, calix[4]arene 24 is much more activated for the electrophilic aromatic substitution, reacts with NO₂/N₂O₄ even faster. Within few minutes, the reaction produced a complex mixture of dealkylated and oxidized products.

![Figure 3.8](image.png)

**Figure 3.8** Left: NO⁺ transfer between calix[4]arene containers, a cartoon representation. Right: formation of complex 39 from complex 24.

For the exchange experiments, we obtained 31 by treating calix[4]arene 21 with 3 equivalents of NO₂/N₂O₄ and 1 eq of SnCl₄ in CHCl₃(CHCl₃) followed by precipitation with hexanes. Further, complex 31 and “empty” host 24 were mixed in a 1:1 ratio at 295 K in dry chloroform, and the UV-vis and ¹H NMR spectra were recorded over two hours (Figure 3.9). Due to the strong affinity of 24 towards NO⁺, the guest presence outside the cavity, in the bulk solution, was considered negligible, and the only source of NO⁺ was 31.

Initially, the ¹H NMR spectrum exhibited only sets of signals for 31 and free calix[4]arene 24, and the corresponding UV-vis spectrum showed only the
characteristic absorption for charge-transfer in 31. Within minutes however, the guest transfer was clearly detected. The band at $\lambda_{\text{max}} \approx 524$ nm, assigned to complex 31, systematically decreased and a new band at $\lambda_{\text{max}} \approx 600$ nm, corresponding to new complex 39, appeared.

![Figure 3.9 UV-vis monitor of NO$^+$ guest transfer: Absorption of complex 31 at 524 nm decreases and new complex 39 absorption at 600nm increase. In the end only complex 39 absorption can be seen.](image)

The NO$^+$ transfer can even be observed visually. The purple solution of 31 in CHCl$_3$ turns blue upon addition of calix[4]arene 24. During UV-vis measurement, the concentration of the complexes is low, the color shows violet and blue for 31 and 39 respectively (Figure 3.9). When followed by $^1$H NMR spectroscopy, the NO$^+$ exchange resulted in clean transformation of the spectra from mixture 31 + 24 to mixture 21 + 39 (Figure 3.10).
Figure 3.10 Portions of the $^1$H NMR spectra (500 MHz, CDCl$_3$, 295 ± 1 K) of: (a) NO$^+$ complex 31, obtained from 21, NO$_2$/N$_2$O$_4$ and SnCl$_4$. (b) mixture of complex 31 and calix[4]arene 24 after 20 min; ~30% conversion to 39. (c) The same mixture after 1 h; complex 39 is formed with >95% conversion. (d) NO$^+$ complex 24·NO$^+$SbF$_6^-$, independently obtained from 24 and NO$^+$SbF$_6^-$· The residual CHCl$_3$ signals are marked as before, the decomposition products of 24 are marked "**".
For example, the methylene bridge CH$_2$ and OCH$_2$ protons of 31, seen as a singlet and a triplet, 1:1, at 3.60 and 3.87 ppm ($J = 7.5$ Hz), slowly decrease in intensity. Instead, two OCH$_2$ triplets at 3.93 and 3.76 ppm ($J = 7.5$ Hz) and the methylene bridge CH$_2$ singlet at 3.44 ppm appear and grow. These were assigned to complex 39 and confirmed in the series of independent experiments between 24 and NO$^+$SbF$_6^-$. Signals for "empty" calix[4]arene 21 also appear, although slightly shifted due to the presence of SnCl$_4$, and signals for 39 disappear. Within an hour the NO$^+$ transfer was completed; both the $^1$H NMR and UV-vis spectra exhibited only the signals of complex 39 and free calix[4]arene 21. No traces of initial complex 31 were detected. To our knowledge, this is the first case of a quantitative guest transfer between two different molecular containers. Such behavior has a potential for information storage and processing since the color can be switched between two distinguishable states (similar to 0, 1 used in binary computation).

3.5 Conclusions

NO$_2$/N$_2$O$_4$ reversibly react with O-alkylated calix[4]arenes with the formation of deeply colored calix[4]arene - NO$^+$ complexes. In these complexes, NO$^+$ is encapsulated inside the $\pi$-electron rich calix[4]arene tunnel and form strong ($K_{assoc} > 10^6$ M$^{-1}$) charge transfer complexes. The color change associated with the formation of complex might be useful in construction of optical sensors selective for NO$_2$/N$_2$O$_4$. The dynamics of complexation process provides a possible way to further utilize the complexes in organic synthesis.
CHAPTER 4
SOLID SUPPORTED CALIX[4]ARENES FOR
ENTRAPMENT OF NO$_2$/N$_2$O$_4$

For potential application in supramolecular chemistry, organic synthesis and sensing technology, receptor molecules must be readily immobilized on solid supports or surfaces.$^{74,75}$

As reagents in organic synthesis, solid supports have a lot of advantages. Solid-supported reagents are easily removed from reactions by filtration. Excess reagents can be used to drive reactions to completion without introducing difficulties in purification. Recycling of recovered reagents is economical, environmentally sound, and efficient. Ease of handling is especially important when dealing with expensive or time-intensive catalysts which can be incorporated into flow reactors and automated processes. Chemical properties can be finely tuned by altering the choice of the support. Toxic, explosive, and noxious reagents are often more safely handled when contained on solid support. Reagents on solid-support react differently, mostly more selectively, than their unbound counterparts.

There are also some disadvantages related to solid supports. Some reagents may not interact well. Ability to recycle reagents on solid support is not assured. Reactions may run more slowly due to diffusion constraints. Polymeric support materials can be
very expensive to prepare. Stability of the support material can be poor under harsher reaction conditions. Side reactions with the polymer support itself may occur.\textsuperscript{74,75}

Solid supports include both organic and inorganic agents. Alumina, silica, zeolites and clays are among the most common inorganic solid supports. Organic solid supports mostly are polymer resins including soluble and insoluble systems. The widely used polyethylene glycols (PEG) are standard examples of soluble polymers in homogeneous reaction conditions. Chloromethylstyrene-divinylbenzene resins (Merrifield resins) are the standard supports for solid phase peptide syntheses and more recently for solid phase organic synthesis.

Making polymer supports can be achieved by grafting onto commercially available polymers or polymerization of functional monomers. Because the availability of commercial polymers is extensive, the first thing to do is to select an appropriate resin. A polymer support can be used to immobilize a reactant or catalyst species. The location of active sites in a network polymer support depends on the type of polymer support. In swollen gel beads, the active sites are evenly distributed. In macroporous beads, they may be predominantly on the internal surface of macropores.

Although a wide variety of polymers are now commercially available, \( \text{NO}_2/\text{N}_2\text{O}_4 \) (and \( \text{NO}_X \) in general) reacts with many of them, causing destruction and aging.\textsuperscript{76} As a free radical, \( \text{NO}_2/\text{N}_2\text{O}_4 \) readily attacks double bonds in polybutadienes, polyisoprenes and their copolymers, ester groups in poly(methyl)methacrylate, and also amide fragments in polyamides and polyurethanes. Furthermore, \( \text{NO}^+ \), generated from various \( \text{NO}_X \) gases, react with alkenes and other double bond-containing structures.\textsuperscript{77}
Polymers resistant to NO\textsubscript{x} include polyethylene glycol, polystyrene, polyethylene. Inert inorganic materials are also appropriate for support purpose. Silica gel is among the selections, not only because it is stable to NO\textsubscript{x}, it is also easy to functionalize.

To be attached to the solid support, calix[4]arenes should bear appropriate functional groups. Synthesis of appropriately functionalized calix[4]arenes will be the first step.

Among the advantages of reagents immobilized on polymeric supports\textsuperscript{78} are the ease of their separation from the reaction mixture, their recycling, and simplification of the handling of toxic and malodorous chemicals. Particularly useful are so-called soluble polymers, as they allow the circumvention of problems associated with the heterogeneous nature of the reaction conditions. At the same time, precipitation can isolate these polymers from the reaction mixture. For the case in hand, the simplification of handling toxic NO\textsubscript{x} gases is of particular importance. Silica gel is easy to functionalize and separate from solution after reaction, and it’s also stable to NO\textsubscript{x} and NO\textsuperscript{+}.

Functionalization of calix[4]arenes and immobilization will be discussed in this chapter. Materials synthesized will be used for NO\textsubscript{x} fixation, storage and release.

\textbf{4.1 Functionalization of \textit{Cone Conformation} Calix[4]arenes}

For the attachment to the solid support, proper functionalization of calix[4]arenes is necessary. We opted for the lower rim mono functionalization of calix[4]arene because it is easier to control the functionalization process.
Scheme 4.1 Preparation of functionalized cone conformation calix[4]arene. a) Br(CH$_2$)$_5$CH$_3$, BaO/Ba(OH)$_2$, DMF, 25 °C, 12 h, 69%. b) BrCH$_2$C(O)OC$_2$H$_5$, Na$_2$CO$_3$, MeCN, 80 °C, 12 h, 89%. c) KOH, THF-H$_2$O, 100 °C, 12 h, then aq HCl, >95%. d) N-hydroxysuccinimide, DCC, DMAP, THF, rt, 12 h, 83%.

Tris-O-propyl substituted cone calix[4]arene with a functional group ready to be attached to the solid support was synthesized according to the Scheme 4.1. Tris-O-substituted calix[4]arene 40, prepared by selective alkylation of the parent calix[4]arene with $n$-propyl bromide and BaO/Ba(OH)$_2$ in DMF (69%),$^7$ was further alkylated with ethyl bromoacetate to afford derivative 41 (Na$_2$CO$_3$, MeCN, 89%) (Scheme 3.1). This was hydrolyzed with KOH in THF-H$_2$O mixture, resulted calix[4]arene acid 42 in a quantitative yield. Acid 42 was further activated with N-hydroxysuccinimide (DCC, DMAP, THF) to afford the activated ester 43 (83%). Compound 43 readily reacted with 3-aminopropyl silica gel with the formation of material 49 (see Scheme 4.4).
4.2 Functionalization of 1,3-Alternate Calix[4]arenes

While lower-rim \(O\)-alkylated and lower-rim \(O\)-benzylated calix[4]arenes are easily formed via simple Williamson-type etherification reactions of the corresponding calix[4]arenes with alkyl or benzyl halides, the syntheses of nonsymmetrical 1,3-alternate \(O\)-alkyl ether analogues were rarely reported. Because of the requirement for inversion of conformation during the synthesis, the selection of the alkylation agent plays an important role. Because the template effect can operate during the alkylation reaction, which can influence the number and position of substituents on the product as well as calixarene conformations,\(^7^9\) alkylation reagents without strong interaction with metal ions should be selected. This will ensure the formation of desired calixarene conformations and numbers of substituents. For this reason, we selected allyl bromide as alkylation reagent. The allyl moiety was introduced before the conformation inversion, and it can be easily modified through functional group interconversion.

The synthesis of terminally functionalized 1,3-alternate calix[4]arenes starts with the preparation of monoalkylated 44, using \(n\)-propyl bromide and an equimolar quantity of \(K_2CO_3\) as a base in boiling MeCN (Scheme 4.2). The resulting calix[4]arene 44\(^8^0\) was further alkylated with allyl bromide to afford diametrically substituted product 45 (\(K_2CO_3\), MeCN, reflux, 67\%). The next step includes formation of calix[4]arene 46, which is a \(Cs^+\)-templated alkylation of 45 with an excess \(n\)-propyl bromide (\(Cs_2CO_3\), MeCN, reflux, 70\%). This reaction proceeds with the conformation conversion from a cone to a 1,3-alternate. The allyl double bond in 46 was hydroxylated under the standard hydroboration conditions (\(BH_3\cdotTHF\), THF, then aq NaOH, \(H_2O_2\)) to afford
calix[4]arene 47 in 95% yield. Compound 47 is the key derivative for preparation of polymer-supported materials for NO$_2$/N$_2$O$_4$ sensing and fixation. It has the structural features of typical 1,3-alternate and also possesses a terminal hydroxyl group for further functionalization.

Scheme 4.2 Synthesis of 1,3-alternate calix[4]arene 47. (a) n-PrBr, K$_2$CO$_3$, MeCN, reflux, 59%; (b) Allyl bromide, K$_2$CO$_3$, MeCN, reflux, 67%; (c) n-PrBr, Cs$_2$CO$_3$, MeCN, reflux, 70%; (d) BH$_3$·THF, THF, then NaOH, H$_2$O$_2$, 95%.

Scheme 4.3 Synthesis of calix siloxane. a) Karstedt cat, HSi(OEt)$_3$, toluene, reflux, 40%.
To be attached to the surface of silica gel, calix[4]arene 46 was converted to siloxane derivative 48, which can easily react with OH groups on the silica gel surface. In the presence of Karstedt catalyst (i.e. Pt$_2$\{[(CH$_2$=CH)Me$_2$Si]$_2$O$_3$\}), 46 was heated with triethoxysilane in toluene for 20 hours to form 48 in 40% yield. The remaining material is the tri propyl partial cone calix[4]arene, due to deallylation by the catalyst.

4.3 Immobilization and Utilization of Supported Calix[4]arene Materials

The first approach towards immobilization was performed with functionalized silica gel (Scheme 4.4). Reaction between 3-aminopropyl silica gel and activated calixarene ester 43 was carried out in THF at room temperature in the presence of triethylamine (TEA) for 12 hours, the resulting silica gel was extensively washed with different solvents to remove the unreacted calix[4]arene and dried at 100 °C in vacuum for 2 days.

Octylamine was used as the model compound in reaction with active ester 43. The reaction was carried out in THF at room temperature in the presence of triethylamine (TEA) for 12 hours. The product was purified by column chromatography to
afford amide bond linked calix[4]arene 50 (Scheme 4.5 65% yield). The characteristic amide N-H bond absorption in IR spectrum at 3346 cm\(^{-1}\) demonstrated the formation of compound 50.

![Scheme 4.5 Coupling of calix[4]arene active ester and octylamine.](image)

The presence of a calix[4]arene fragment in 49 was confirmed by the FTIR analysis in KBr disks. \(\nu\)(Ar-H) \(\approx\) 2960 cm\(^{-1}\) and \(\nu\)(C=O) \(\approx\)1650 cm\(^{-1}\) were recorded, which are similar to the stretching of model calixarene amide 50: \(\nu\)(CH) = 2964 cm\(^{-1}\) and \(\nu\)(C=O) = 1680 cm\(^{-1}\). From the CHN analysis, only \(\sim\)17% (17% total NH\(_2\) in silica gel) calixarene loading was achieved, which may be due to the steric bulkiness of the calixarene fragment.

In the NO\(_2\)/N\(_2\)O\(_4\) entrapment experiments, a stream of the gas was passed through Pasteur pipettes loaded with silica gel 49 (Figure 4.1). One pipette was loaded with dry silica gel 49, and the other contained 49 pre-wetted with CHCl\(_3\). Both silica gels instantly turned dark purple, indicating the NO\(^+\) complexation. The color of the wetted material appeared to be deeper and it stayed for 2-3 h. The dry material bleached within minutes. The FTIR spectrum, recorded in KBr disks, gave weak but reproducible
stretch at $v \approx 1920$ cm$^{-1}$, indicating the presence of arene-NO$^+$ complexes. No coloration was observed for the pipet loaded with the starting, 3-aminopropylated silica gel. This once again emphasizes the role of calix[4]arene cavities in the described processes.

Figure 4.1 NO$_2$/N$_2$O$_4$ entrapment "chromatography" experiments. The columns were prepared as follows: (a) loaded with starting aminopropyl functionalized silica gel; (b) loaded with dry silica gel 49; (c) loaded with 49 and flashed with CHCl$_3$. All three columns were then flashed with NO$_2$/N$_2$O$_4$ (~30 s), and the pictures were made after ~2-3 min afterward.

Although requiring further synthetic optimization, silica gel 49 may still be used for NO$_2$/N$_2$O$_4$ detection and even for purification of other NOx, especially NO. To be used as nitrosating reagent, the solid support materials must be stable at reaction condition. Silica gel 49 has an amide bond which can react with NO$_2$/N$_2$O$_4$, and
subsequently be broken. Making the linker an ether bond can avoid this problem, because the ether bond is stable to both NO$_2$/N$_2$O$_4$ and NO$^+$. 

Following our work, Economy’s group (Figure 4.2) synthesized calix[4]arene-based periodic mesoporous organosilica (silica gel - calix[4]arene) by sol-gel techniques. Their results showed that the material in dry state can store NO$_2$ and may be useful in sensing and storing of NO$_2$.

To improve the loading, appropriate silica gel selection can achieve the goal easily. High porosity silica gel has higher surface area thus can provide higher loading of calix[4]arene. The larger channel in the porous material can also provide a pathway for the substrate to approach the reaction center, i.e. encapsulated NO$^+$. 

![Figure 4.2 Calix[4]arene-based periodic mesoporous organosilica.](image)
commercial silica gel of higher porosity (150 Å, Aldrich) was activated with 18% HCl at reflux and then treated with calix[4]arene siloxane 48 in CH₂Cl₂ to give material 51 (Scheme 4.6). The presence of calix[4]arene units in 51 was confirmed by the appearance of characteristic calix[4]arene absorption bands in the IR spectrum at for example ν = 2965, 1470, 1106 cm⁻¹. From the thermogravimetric analysis (TGA) and CHN analyses, the calix[4]arene loading of ~10% (weight) was estimated. Such a rather modest number appeared to be reproducible, even when larger quantities of 48 were employed, and may be due to the steric bulkiness of the calix[4]arene fragment.

In the NO₂/N₂O₄ entrapment tests, NO₂/N₂O₄ was bubbled through the suspension of 51 in CH₂Cl₂ for 10 sec. The dark blue solid was filtered and washed with dry CH₂Cl₂ to afford complex 52. The characteristic IR absorption at ν = 1945 cm⁻¹ shows the presence of NO⁺ in the material. The deep blue color showed the entrapment of NO⁺ in the cavity of calixarene(Figure 4.3).
Soluble solid supports were also prepared. Considering the recovery of the reagent, polyethylene glycol is an ideal selection. Apparent reasons are that it will not react with NO$_2$/N$_2$O$_4$, and the PEG supported reagent is relatively easily precipitated from the solution by adding diethyl ether or hexanes.

Scheme 4.7 Synthesis of PEG supported calix[4]arenes and complex formation with NO$_2$/N$_2$O$_4$. a) CH$_2$Cl$_2$, Et$_3$N, 0°C, 2 h; b) CH$_2$Cl$_2$, rt. 12 h, 55% loading.
Mesylation of mono methoxy polyethyleneglycol 53 (MW = 5000, Fluka, Inc.) by methanesulfonyl chloride in dry CH$_2$Cl$_2$ at 0 °C in the presence of Et$_3$N afforded 54 in quantitative yield. Coupling of 54 and calix alcohol 47 in CH$_2$Cl$_2$ afforded PEG supported material 55 at 55% loading. NO$^+$-storing polymer 56 (Scheme 4.7) was prepared upon bubbling NO$_2$/N$_2$O$_4$ through the solution of 44 in CH$_2$Cl$_2$ for 2-3 min, followed by bubbling N$_2$ for 10 min to remove the remaining NO$_2$/N$_2$O$_4$ gases.

Figure 4.4 NO$_2$/N$_2$O$_4$ entrapment experiments: The columns were prepared as follows: a. loaded with starting PEG monomethyl ether (Fluka); b. loaded with dry polymer 55; c. loaded with 55 and washed with hexanes. All three columns were then flushed with NO$_2$/N$_2$O$_4$ for 30 seconds.

Entrapment of NO$_2$/N$_2$O$_4$ gases was performed as described in Figure 4.4. Both the dry polymer and pre-wetted polymer have changed color when passing NO$_2$/N$_2$O$_4$
gases through the pipette. Polyethylene glycol has no color change upon after NO₂ passed through the pipette. This is also a visual demonstration of calix[4]arene - NO⁺ complex formation.

4.4 Conclusions and Outlook

Solid supported calixarenes were synthesized for entrapment of NO₂/N₂O₄. Upon reaction with NO₂/N₂O₄, these materials complex NO⁺ in dry solid state and solution (suspension) with an apparent color change. The NO⁺ complexes are stable for 2 - 3 hours, which is important for NO₂/N₂O₄ storage and utilization. Further exploration of the supported materials in homogeneous and heterogeneous organic syntheses will be described in the next chapter.
CHAPTER 5
ENCAPSULATED NITROSATING REAGENT

5.1 Nitrosating Reagents and Mechanism

In organic chemistry, nitrosation holds a special place. Alkynitriles (RO-NO), nitrosamines/amides, and nitrosothiols are used in biomedicine as NO-releasing drugs.\textsuperscript{83} In organic synthesis, -N=O is an important activating group, allowing elegant transformations of amides to carboxylic acids and their derivatives.\textsuperscript{84} In addition, nitrosation mimics interactions between biological tissues and environmentally toxic NO\textsubscript{X} gases, which generate mutagenic nitrosamines/peptides and nitrosate and deaminate DNA.\textsuperscript{16}

It is known that reactions between NO\textsuperscript{+} generating agents (e.g., NOCl, N\textsubscript{2}O\textsubscript{3}, NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4}, NO\textsuperscript{+} salts, etc.) and amides and short peptides proceed via N-nitrosation and yield biologically important nitroso-derivatives.\textsuperscript{83,85} Nitrosation of peptides may be used in analytical protocols of protein sequencing in the future. More importantly however, these reactions have a biological relevance, because NO\textsubscript{X} are widely spread atmospheric pollutants and frequently interact with biological tissues and fluids.\textsuperscript{86}

In the previous chapters, we described processes involving chemical fixation of NO\textsubscript{2}/N\textsubscript{2}O\textsubscript{4}, its conversion to encapsulated NO\textsuperscript{+} complexes, and subsequent NO\textsuperscript{+} transfer to electron rich substrates. We noticed that primary and secondary amides also react
with calix[4]arene - NO⁺ complexes, which implies that these complexes may act as nitrosating reagents.

![Diagram of supramolecular fixation of NOₓ gases: Encapsulated nitrosating reagents.](image)

Figure 5.1 Supramolecular fixation of NOₓ Gases: Encapsulated Nitrosating reagents.

In this chapter, we introduce novel nitrosating reagents, which are based on calix[4]arene - NO⁺ complexes. We define **encapsulated nitrosating reagents** (Figure 5.1) as highly reactive species, for example NO⁺, reversibly entrapped within the host cavity that can be released into the reaction mixture under subtle control. The cavity offers protection from the bulk environment and thus controls the reaction rates. Chemical transformations with encapsulated reagents may occur either within the cavity.
interior, or outside, upon release. For such complexes, stabilization of reactive species within the interiors, \(^{87}\) controlled chemical reactivity, \(^{88}\) and catalysis \(^{89}\) have been impressively demonstrated. As far as the delicate, noncovalent forces holding the molecule-within-molecule complex together are concerned, temperature, solvent polarity, and substrate-cavity size-shape complementarities are the critical factors responsible for the reagent release and the occurrence of the reaction. Here, we introduce a novel class of encapsulated reagents, stable, mild and selective nitrosating reagents that are based on reversible encapsulation of reactive NO\(^+\) species by calix [4] arenes such as complex 35.

![Scheme 5.1 Nitrosation of amides.](image)

We determined that secondary amides can react with encapsulated nitrosating reagent to form nitrosoamide (Scheme 5.1). Complex 35 is used to react with different amides, the results are listed in table 5.1.

For the preparation, 1,3-\textit{alternate} based NO\(^+\) complex 35 was mixed with 57a-e (RC(O)NHMe, R = n-Et, n-Pr, n-But, n-Pent, n-Hex, n-Hept) in dry CHCl\(_3\) and stirred
Figure 5.2 $^1$H NMR analysis of nitrosation reactions (500 MHz, CDCl$_3$, 295 ± 1 K): (A) $N$-nitrosoamides 58b (left) and 58c (right), independently obtained from 57b,c and NO$_2$/N$_2$O$_4$, respectively; (B) reaction mixtures 35 + 57b (left) and 35 + 57c (right) after ~1 h; and (C) guest-free calix[4]arene 27.

at room temperature. Dark-blue solutions of 35 quickly discharged upon addition, which is a reasonable visual test for the reaction. In the $^1$H NMR spectra of the reaction
mixtures, signals for amides 57a-e and complex 35 disappeared and new, characteristic signals for N-nitrosoamides at ~3.2 ppm (2 H, q for 57a and t for 57b-e, C(O)CH₂) and ~3.1 ppm (s, 3 H, N(NO)-CH₃) and for NO⁺-free calix[4]arene 35 were detected (Figure 5.2). The corresponding N-nitrosoamides RC(O)N(NO)Me (58a-e) were formed in 50-95% yield. At the same time, when 57f-q was mixed with calix[4]arene - NO⁺ complexes under the same conditions, no decoloration occurred, and NMR spectroscopy showed no nitrosoamide produced.

In reaction with a variety of amides 57a-q, only those possessing N-CH₃ substituents were transformed to the corresponding N-nitrosoamides 58a-e. No reaction occurred for substrates 57f-q (Table 5.1, NMR analysis). Accordingly, no color discharge was observed for these reaction mixtures.

Table 5.1 Nitrosation of amides 57a-57q with encapsulated reagent 35 and yields of N-Nitrosoamides 58a-58q (detected by NMR spectroscopy, reaction mixture)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>R’</th>
<th>Yield, %</th>
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<tr>
<td>57a</td>
<td>C₂H₅</td>
<td>CH₃</td>
<td>50</td>
</tr>
<tr>
<td>57b</td>
<td>CH₃(CH₂)₂</td>
<td>CH₃</td>
<td>68</td>
</tr>
<tr>
<td>57c</td>
<td>CH₃(CH₂)₃</td>
<td>CH₃</td>
<td>53</td>
</tr>
<tr>
<td>57d</td>
<td>CH₃(CH₂)₄</td>
<td>CH₃</td>
<td>95</td>
</tr>
<tr>
<td>57e</td>
<td>CH₃(CH₂)₆</td>
<td>CH₃</td>
<td>63</td>
</tr>
<tr>
<td>57f</td>
<td>C(CH₃)₃</td>
<td>CH₃</td>
<td>&lt; 5</td>
</tr>
</tbody>
</table>
Table 5.1 - continued

<p>| | | | |</p>
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<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>57g</td>
<td>C₂H₅</td>
<td>C₂H₅</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>57h</td>
<td>CH₃(CH₂)₂</td>
<td>C₂H₅</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>57i</td>
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</tr>
<tr>
<td>57j</td>
<td>CH₃(CH₂)₄</td>
<td>C₂H₅</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>57k</td>
<td>C₂H₅</td>
<td>CH₃(CH₂)₂</td>
<td>&lt; 5</td>
</tr>
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<td>CH₃(CH₂)₂</td>
<td>CH₃(CH₂)₂</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>57m</td>
<td>CH₃(CH₂)₃</td>
<td>CH₃(CH₂)₂</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>57n</td>
<td>CH₃(CH₂)₄</td>
<td>CH₃(CH₂)₂</td>
<td>&lt; 5</td>
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<tr>
<td>57o</td>
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<td>CH(CH₃)₂</td>
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<tr>
<td>57p</td>
<td>C(CH₃)₃</td>
<td>C(CH₃)₃</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>57q</td>
<td>CH₃(CH₂)₃</td>
<td>CH₂C₆H₅</td>
<td>&lt; 5</td>
</tr>
</tbody>
</table>

Such delicate selectivity of \(N\)-nitrosation by complex 35 was unexpected and may be due to steric effects. Clearly, the unreacted substrates were those possessing \(N\)-alkyl groups bulkier than CH₃.
Figure 5.3 Currently accepted mechanism of \( N \)-nitrosation of secondary amides\(^8\) and proposed mechanism of nitrosation with encapsulated calix[4]arene based reagent.

\( \text{NO}^+ \) is an aggressive electrophile and its reaction is typically not selective.\(^9\)

Mechanistically, nitrosation of secondary amides and peptides incorporates an electrophilic attack of \( \text{NO}^+ \) (generated from \( \text{NO}^+ \)-salts, \( \text{N}_2\text{O}_3 \), or \( \text{NO}_2/\text{N}_2\text{O}_4 \)) on a nucleophilic carbonyl oxygen of the substrate, yielding the corresponding \( O \)-nitroso species (Figure 5.3).\(^9\) Rapid deprotonation, rotation around the C-O bond, and the \textit{cis}-\textit{trans} inversion through the nitrogen results in an intermediate, in which both the nitrogen lone pair and the \(-\text{N}=\text{O}\) group are properly oriented for the isomerization to the \( N \)-nitrosoamide. Dimensions and shapes of the amide R and R’ become much more
crucial when encapsulated reagents are employed. The substrate 57 approaches the
cavity facing it with the carbonyl oxygen atom (Figure 5.3, bottom). One scenario
places the N-R’ alkyl group close to the two t-Bu and two alkoxy groups of the
calix[4]arene. For larger R’, this could be sterically unfavorable, so that the substrate
C=O and the encapsulated NO⁺ would not reach each other. The alkyl group on
carbonyl of substrates 57 is apparently positioned farther away from the calix[4]arene
substituents and does not significantly interfere, except in the case with bulky amide 57f
(Table 5.1).

Once formed, the O-nitroso intermediate leaves the interior and, as expected,
further collapses in bulk solution (Figure 5.3, top). Due to the extremely strong binding
of NO⁺ by the calix[4]arene ($K_{assoc}>10^8$ M⁻¹), the rate-limiting formation of the O-
nitrosation intermediates should take place within the cavity, prior to the NO⁺
dissociation. Otherwise, all reactions should proceed with the similar rate, and no
selectivity should be observed. Currently used nitrosating agents such as HNO₂, NOCl,
N₂O₃, NO₂/N₂O₄, NO/O₂, NO/air, and nitrosonium salts are typically not selective. This
once again emphasizes the role of supramolecular effects in encapsulating nitrosating
reagents.

The size and shape of the calix[4]arene together with the substituents on it
generate steric effects, and result in the repulsive interactions between the container and
the substrates, leading to the observed size - shape selectivity.

Under the same conditions, the cone calix[4]arene complex 29 reacted very
slowly, and only traces of the N-nitrosoamide products were detected by $^1$H NMR
spectroscopy. t-Bu groups at the upper rim of 29 impose steric hindrances and protect the encapsulated NO$^+$ species from the substrate. The rate limiting formation of the nitroso intermediates, can not take place within the calix[4]arene cavity, thus the reaction is very slow.

5.2 Chiral Calix[4]arenes Syntheses and Reaction with Chiral Amides

Chiral calix[4]arenes 61 and 62 were prepared, which posses 2-(S)-(+)methylbutyl fragments attached to one or both calix[4]arene rims, respectively (Scheme 5.2). NO$^+$ complexes 63 and 64 were then generated from NO$_2$/N$_2$O$_4$, which may be considered as chiral encapsulating reagents. In the preliminary experiments, these complexes were used in reaction with a racemic secondary amide. Preference for one enantiomer of the amide over the other was expected, as the reaction takes place at the chiral calix[4]arene rim.

![Scheme 5.2](image)

59 \( R = (CH_2)_6CH_3 \)

60 \( R = (S)-(+)CH_2CH(CH_3)CH_2CH_3 \)

61 \( R = (CH_2)_6CH_3, R' = (S)-(+)CH_2CH(CH_3)CH_2CH_3 \)

62 \( R, R' = (S)-(+)CH_2CH(CH_3)CH_2CH_3 \)

Scheme 5.2 Preparation of chiral 1,3-alternate calix[4]arene. a) n-HexBr, K$_2$CO$_3$, MeCN, reflux, 60% for 59 and 1-bromo-2-(S)-(+)methylbutane, K$_2$CO$_3$, MeCN, reflux, 50% for 60; b) n-HexBr, Cs$_2$CO$_3$, MeCN, reflux, 42% for 61 and 1-bromo-2-(S)-(+)methylbutane, Cs$_2$CO$_3$, MeCN, reflux, 15% for 62.
When added to a solution of the racemic $N$-methylamide of 3-methylvaleric acid $(R,S)$-65 ($\sim$5-10 equiv excess) in freshly distilled CH$_2$Cl$_2$, complexes 63 and 64 readily react. The dark-blue color disappeared in 1-2 h, yielding mixtures of $(R)$- and $(S)$-66 in 60-80% total yield (1H NMR spectroscopy). The products were then purified by column chromatography. Initially, 10 equivalents of chiral solvating agent (Pirkle’s reagent, (-)-(2,2,2-trifluoro-1-(9-anthryl)ethanol (Acros)) was applied to determine the enantiomeric excess $(ee)$. However, no separation of the diastereomeric solvates was detected by 1H NMR spectroscopy; this is, most probably, due to insufficient intermolecular interactions.

![Diagram of chiral calix[4]arene - NO+ complexes 63, 64 formation and nitrosation of racemic amide 65.](image)

Scheme 5.3 Chiral calix[4]arene - NO$^+$ complexes 63, 64 formation and nitrosation of racemic amide 65.

For the enantiomeric excess $(ee)$ determination, the obtained $N$-nitroso products $(R)$-66 and $(S)$-66 were quantitatively converted back to 65 with TFA. In this case, addition of the Pirkle’s reagent to a solution of a mixture $(R)$- and $(S)$-65 in C$_6$D$_6$ readily
Figure 5.4 $^1$H NMR analysis of nitrosation reactions between chiral complexes 63, 64 and racemic amide 65. A) Mixture of amides (R)-65 and (S)-65, obtained after the reaction with complex 63; no ee was detected. Identical spectrum was obtained for independently synthesized, racemic 65 with the Pirkle’s reagent. B) Mixture of amides (R)-65 and (S)-65, obtained after the reaction with 64; ≈15% ee was detected, with the preference for the (S)-configuration. C) Proposed intermediate for chiral reaction between complex 64 and racemic amide 65.
produced two sets of signals for the mixture. These were used to determine the ee in nitrosation with 63, 64, and the stereoisomers distribution was analyzed with (Pirkle’s reagent, 500 MHz, C₆D₆) (Figure 5.4).

While reaction between reagent 63 and racemic amide 65 did not result in chiral discrimination, modest but reproducible ~ 15% ee of (S)-N-nitrosoamide 65 versus (R)-N-nitrosoamide 66 was obtained for reagent 64. Geometry of pre reactive complexes 63-65 is, most probably, similar to the complex 64-65 (see Figure 5.4). In the proposed scenario, molecule 65 approaches the cavity 64 facing it with the carbonyl oxygen atom, thus placing the C(O)CH₂CH₂EtMe group in close proximity to the calix[4]arene rims' chiral OCH₂C*HEtMe groups. Van der Waals contacts occur, and chiral discrimination results. In the case of calix[4]arene 63, possessing one rim with a chiral OCH₂C*HEtMe fragment and the other with O(CH₂)₅CH₃ group, the substrate apparently chooses the latter, less hindered site. Consequently, no stereoselectivity is observed.

Despite being modest, the stereoselectivity offered by chiral nitrosating reagent 64 is novel. Indeed, all currently employed sources of NO⁺ are achiral. To improve the ee values, further structural modification of calix[4]arenes is required; this includes placement of the chiral groups much closer to the reaction center. In the future, thermal decomposition of enantiomerically enriched or pure N-nitrosoamides could lead to chiral carboxylic acids and their derivatives. Exploration of these features may help to design optically active NO donors.
5.3 Nitrosation with Solid Supported Calix[4]arene

In the previous chapters, polyethylene glycol supported calix[4]arene - NO\(^+\) complex 56 and silica gel supported calix[4]arene - NO\(^+\) complex 52 were described. They will now be used in nitrosating of secondary amides.

The reaction between 57 and complex 56 was performed in a homogeneous phase. When their solutions in CH\(_2\)Cl\(_2\) were added equimolar solutions of amide 57e, 67a-b (CH\(_3\)(CH\(_2\))\(_6\)C(O)NHR, R = Me, Et, Pr, respectively), they reacted quickly (2-3 h) at room temperature, yielded corresponding N-nitrosoamides 58e, 68a-b (Figure 5.5). The solution's color discharged, thus visually indicating the reaction progress. Polymer 55 was subsequently recovered by precipitating with hexanes and filtered off. Yields of nitrosoamides 58e, 68a-b were determined by \(^1\)H NMR spectroscopy, integrating signals of the product vs. the starting compounds.82
Signals for amides 57e, 67a-b decrease, and characteristic signals for N-nitrosoamides 58e, 68a-b appear and grow. For example, a triplet at 3.2 ppm (C(O)CH₂) and a singlet at 3.1 ppm (N(NO)-CH₃) were clearly registered for nitrosoamide 58e; these were identical to those obtained upon nitrosation of 46a with neat NO₂/N₂O₄ and different from the starting amide 57e (Figure 5.6).

Figure 5.6 Fragments of the ¹H NMR spectra (500 MHz, CDCl₃, 295±1 K): (A) N-methylamide 57e; (B) N-methyl-N-nitrosamine 58e obtained from 57e and NO₂/N₂O₄; (C) N-methyl-N-nitrosamine 58e obtained from 57e and polymer 56.
After at least five runs, the averaged yields of nitrosoamides $58e$, $68a-b$ varied between 40% for $68b$ to 60% for $68a$ and 80% for $58e$; which indicate the preference for less bulky substrates. At the same time, polymeric reagent $56$ is obviously less size-shape selective, compared to monomeric species, which showed exclusive selectivity for smaller $N$-Me derivative $57e$. In control experiments involving starting PEG polymer and amide $57e$, only trace amounts of $58e$ were detected (<5%), again emphasizing the role of calix[4]arene cavity in the described reaction.

The dark-blue NO$^+$-storing silica gel $52$ was prepared upon bubbling NO$_2$/N$_2$O$_4$ through the suspension of $51$ in CH$_2$Cl$_2$ for 5-10 s, followed by filtration and washing with CH$_2$Cl$_2$. Material $52$ is quite robust and does not change the color for one week.

$$"\text{Figure 5.7 Nitrosation of amides } 57e, 67a-b \text{ with material } 52."$$
For nitrosation, 52 was suspended in dry CH2Cl2, an equimolar amount of amides 57d, 57e, 57j, 57n or 67a-b was then added, and the reaction mixture was stirred at room temperature for 24 h. The reaction's color discharged, thus visually indicating the reaction progress. Material 51 was separated by simple filtration. Yields of nitrosoamides 58d, 58e, 58j, 58n and 68a-b were determined by 1H NMR spectroscopy, integrating signals of the product versus the starting compounds (Table 5.2).

Table 5.2 Nitrosation of amides by silica gel supported calix[4]arene - NO⁺ complex 52

<table>
<thead>
<tr>
<th>Reaction Mixture</th>
<th>R’</th>
<th>R</th>
<th>Yield of N-nitrosoamide %</th>
</tr>
</thead>
<tbody>
<tr>
<td>57d</td>
<td>CH₃</td>
<td>(CH₂)₄CH₃</td>
<td>22</td>
</tr>
<tr>
<td>57e</td>
<td>CH₃</td>
<td>(CH₂)₆CH₃</td>
<td>40</td>
</tr>
<tr>
<td>57j</td>
<td>C₂H₅</td>
<td>(CH₂)₄CH₃</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>67a</td>
<td>C₂H₅</td>
<td>(CH₂)₆CH₃</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>57n</td>
<td>(CH₂)₂CH₃</td>
<td>(CH₂)₄CH₃</td>
<td>8</td>
</tr>
<tr>
<td>67b</td>
<td>(CH₂)₂CH₃</td>
<td>(CH₂)₆CH₃</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>Silica Gel + 57e</td>
<td>CH₃</td>
<td>(CH₂)₆CH₃</td>
<td>&lt; 5</td>
</tr>
</tbody>
</table>

The size-shape selectivity trend, observed for the solution experiments with calix[4]arene - NO⁺ complexes, was clearly seen in this case as well. After at least three independent runs, the averaged yields of N-Me nitrosoamides 58d, 58e were established up to 40%, while bulkier N-Et 57j, 67a and N-Pr derivatives 57n, 67b, formed in much smaller quantities (<8%). In control experiments, involving starting silica gel, no visible
amounts nitroso amides were seen, again emphasizing the role of calix[4]arene cavity in the described reaction.

In future studies, the calix[4]arene loading must be increased, so the yields can be further improved for selective nitrosation. Another important issue is the material stability and regeneration. At this stage, regenerated silica gel 69 showed modest NO\(^+\) storing ability. The saturation with NO\(_2\)/N\(_2\)O\(_4\) characteristically resulted in a deep-blue color; however, this disappeared within 3 - 4 hours. Nitrosation reactions with the regenerated material 69 have rather low yield. Partial nitration of the calix[4]arene units in 52 may be the reason, as the stabilizing SnCl\(_4\) was not used. Silica gel with lower porosity (60 Å) was also tested. The dark-colored NO\(^+\) material was readily formed upon bubbling with NO\(_2\)/N\(_2\)O\(_4\), but showed low reactivity. Multiple hydroxyl groups in silica gels may react with the stabilizers, that is, Lewis acids, and also quench NO\(^+\) reactive species. Partial nitration of the calix[4]arene units in 52 may occur.\(^{43}\) In the meantime we have noticed that the high affinity of 51 and its relatives to the NO\(^+\) species may be very useful for entrapment and utilization of NO\(_x\) gases in general, especially for synthetic and biomedical purposes.

5.4 Conclusions

Novel nitrosating reagents are now available that can be obtained upon fixation of NO\(_2\)/N\(_2\)O\(_4\) with calix[4]arenes. These are encapsulated reagents, and their reactivity and selectivity is controlled by the host cavity. They are stable, mild, and size-shape selective. The first chiral nitrosating reagents are also in hand; this opens doors for stereoselective synthesis of various nitroso derivatives and their transformations. To
test these encapsulated reagents in optimized synthesis of NO-releasing pharmaceuticals, further synthetic modifications of the calix[4]arene cage are required. Another attractive advantage is solid-supported encapsulated nitrosating reagents, which greatly expand the scope of reactions. Having high affinity to NO\(^+\) species, generated by a number of NO\(_x\) gases, these supramolecular materials may be very useful for NO\(_x\) entrapment and separation in biomedical areas. Our findings clearly demonstrate that concepts and techniques of supramolecular chemistry can be applied for conversion of environmentally important gases.\(^5,94\)
CHAPTER 6
EXPERIMENTAL SECTION

6.1 General Information

All of the reagents were purchased from commercial suppliers (Aldrich, Fluka, and Acros) and were used without purification unless otherwise specified.

Melting points were determined on a Mel-Temp apparatus (Laboratory Devices, Inc.) or a Buchi apparatus and are uncorrected.

$^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ at 22 ± 1 °C, unless stated otherwise, on a JEOL Eclipse 500 MHz spectrometer. Chemical shifts were measured relative to residual non-deuterated solvent resonances.

FTIR spectra were recorded on a Bruker Vector 22 FTIR spectrometer using KBr pressed pellet for solids or solution between NaCl plates and reported in cm$^{-1}$.

UV-vis spectra were measured on a JASCO V-530 spectrophotometer.

Matrix-assisted laser desorption/ionization mass spectrometry (MALDI-TOF) was performed on a Bruker BiFLEX I linear time-of-flight mass spectrometer operated in delayed extraction mode.

Elemental analysis was performed on a Perkin-Elmer 2400 CHN analyzer.

For column chromatography, Silica Gel 60 Å (Sorbent Technologies, Inc.; 200-425 mesh) was used.
All experiments with moisture- or air-sensitive compounds were run in freshly distilled, anhydrous solvents under a dried nitrogen atmosphere.

Molecular modeling was performed using MacroModel 7.1.95

Parent tetrahydroxycalix[4]arenes were prepared according to the published procedures.96,97 NO2/N2O4 was generated from copper and concentrated nitric acid.

6.2 Experimental Section

(Carbonyl)(meso-tetra-p-tolylporphyrinato)Ru(II) [Ru(TTP)(CO)] (14). To a solution of Ru3(CO)12 (656 mg, 1.50 mmol) in decalin (30 mL), TTP 13 (500 mg, 0.75 mmol) was added, the resulting solution was heated at 190 °C under nitrogen for 12 h, solvent was evaporated and the resulting solid was purified by chromatography to afford 14 (558 mg 95%): mp > 300 °C; 1H NMR (CDCl3, 25oC) δ 8.70 (s, 8 H), 8.08 (dd, J = 7.7 Hz, J = 1.9 Hz, 4 H), 8.01 (dd, J = 7.7 Hz, J = 1.9 Hz, 4 H), 7.53 (d, J = 8.0 Hz, 4 H), 7.51 (d, J = 7.7 Hz, 4 H), 2.69 (s, 12 H). These data are in agreement with previously published data.98

Nitrato(nitrosyl)(meso-tetra-p-tolylporphyrinato)Ru(II) [Ru(TTP)(NO)(ONO2)] (15). Procedure 1: The NO2/N2O4 stock solution in CH2Cl2 (3.00 mL, 0.46 mmol) was added dropwise to the solution of porphyrin 14 (100 mg, 0.13 mmol) in CH2Cl2 (10 mL), and the reaction mixture was further stirred for 30 min. The solvent was evaporated in vacuum to yield 15 as a dark-green solid. (105 mg, 97%).

Procedure 2: To the solution of Ru(TTP)(NO)Cl 17 (20 mg, 0.024 mmol) in CH3CN-benzene, 1:1 (20 mL) AgNO3 (6 mg, 0.036 mmol) was added with stirring. The solution
was stirred for additional 30 min, after which the precipitated AgCl was filtered through Celite. The solvent was evaporated in vacuum to afford 15. (19 mg 95%). mp >320 °C. 

$^1$H NMR $\delta$ 9.08 (s, 8 H), 8.16 (d, $J = 7.5$ Hz, 4 H), 8.13 (d, $J = 7.5$, 4 H), 7.61 (d, $J = 8.0$ Hz, 8 H), 2.73 (s, 12 H); FTIR (KBr, v, cm$^{-1}$) 1852 s, 1515 m, 1269 s, 950 m; UV-vis ($\lambda_{\text{max}}$, nm) 412, 564; HRMS (MALDI-FTMS, m/z): 800.1969, 770.1996. Calc for C$_{48}$H$_{36}$N$_6$O$_4$Ru: 800.2000 (M - NO$_3^-$), 770.2000 (M - NO$_3^-$ - NO$^+$). These data are in agreement with previously published data.$^{54}$

**Nitrito(nitrosyl)(meso-tetra-$p$-tolylporphyrinato)Ru(II) Ru(TTP)(NO)(ONO) (16).**

A round-bottom flask is charged with 17 (25 mg, 0.03 mmol) dissolved in CH$_3$CN-benzene 1:1 (20 mL), AgNO$_2$ (6.9 mg, 0.045 mmol) is then added with stirring. AgCl precipitated immediately, the reaction is stirred for additional 20 min before the AgCl is removed by passing the mixture through Celite. All solvents were removed in vacuo, and the residue was taken up in CH$_2$Cl$_2$ and then purified by flash chromatography on a silica gel column. Recrystallization from CH$_2$Cl$_2$/hexanes, affords 16 (15.2 mg, 60%): 

$^1$H NMR (C$_6$D$_6$) $\delta$ 9.15 (s, 8 H), 8.10 (dd, $J = 7.5$ Hz, $J = 1.8$ Hz, 4 H), 7.81 (dd, $J = 7.5$ Hz, $J = 1.8$ Hz, 4 H), 7.26 (d, $J = 7.5$ Hz, 4 H), 7.20 (d, $J = 7.5$ Hz, 4 H), 2.38 (s, 12 H). These data are in agreement with previously published data.$^{54}$

**25,26,27,28-Tetrakis($n$-hexyloxy) - calix[4]arene (18).** To a suspension of NaH (120 mg, 5.0 mmol) in DMF (20 mL) was added in small portions calix[4]arene (0.48 g, 1.0 mmol). After 1 h, $n$-hexylbromide (0.72 mL, 5.0 mmol) was added slowly. After the
formation of foam ceased, the mixture was heated to 60 °C and stirred for 18 h. The reaction mixture was allowed to cool to room temperature and then poured into ice/water and filtered. The residue was dissolved in CH₂Cl₂ (50 mL) and washed with a saturated NaCl solution (2 X 20 mL) and water (2 X 20 mL). After drying over MgSO₄, the organic layer was concentrated in vacuo. Trituration of the crude product with MeOH afforded 18 (0.57g, 75%). mp 121 - 123 °C. ¹H NMR δ 6.59 (m, 8 H), 4.45 (d, J = 12.4 Hz, 8 H), 3.87 (t, J = 7.6 Hz, 8 H), 3.13 (d, J = 12.4 Hz, 8 H), 1.90 (m, 8 H), 1.35 (m, 24 H), 0.93 (t, J = 6.6 Hz, 12 H).

25,27-Bis(n-hexyloxy)-26,28-hydroxycalix[4]arene (20). To a suspension of 25,27,26,28-tetrahydroxycalix[4]arene (4.24 g, 0.01 mol) and K₂CO₃ (4.2 g, 0.03 mol) in MeCN (200 mL) n-hexylbromide (4.2 mL, 0.03 mol) was added, and the reaction mixture was refluxed under nitrogen for 48 h. The precipitate was filtered off, and the solution was evaporated to dryness. The residue was redissolved in CH₂Cl₂ (200 mL), and the solution was washed with water (3 x 150 mL) and dried over MgSO₄. After evaporation, the solid residue was treated with MeOH (200 mL) to yield pure 20 as a white solid (5.0 g, 84%). ¹H NMR δ 8.23 (bs, 2 H), 7.06 (d, J = 8.0 Hz, 4 H), 6.91 (d, J = 8.0 Hz, 4 H), 6.73 (t, J = 8.0 Hz, 2 H), 6.65 (t, J = 8.0 Hz, 2 H), 4.32 (d, J = 13.0 Hz, 4 H), 4.00 (t, J = 7.5 Hz, 4 H), 3.37 (d, J = 13.0 Hz, 4 H), 2.1-2.0 (m, 4 H), 1.75-1.7 (m, 4 H), 1.45-1.4 (m, 8 H), 0.95 (t, J = 7.5 Hz, 6 H).
25,26,27,28-Tetra(n-hexyloxy)calix[4]arene-1,3-alternate (21). To a suspension of 20 (5.92 g, 0.01 mol) and Cs₂CO₃ (50 g, 0.15 mol) in MeCN (300 mL) n-hexylbromide (5.74 mL, 0.04 mol) was added, and the reaction mixture was refluxed under nitrogen for 48 h. After cooling, the precipitate was filtered off and treated with a mixture of water (100 mL) and CH₂Cl₂ (100 mL). The organic layer was separated, washed with water (2 x 100 mL), dried over MgSO₄, and evaporated. The residue was recrystallized from MeOH-CHCl₃, 10:1 to give pure 21 (3.50 g, 46%). mp 117-119 °C. ¹H NMR δ 6.98 (d, J = 7.5 Hz, 8 H), 6.68 (t, J = 7.5 Hz, 4 H), 3.62 (s, 8 H), 3.54 (t, J = 7.5 Hz, 8 H), 1.56 (m, 8 H), 1.32 (m, 24 H), 0.92 (t, J = 7.5 Hz, 12 H); MALDI-TOF MS m/z 783.9 ([M+Na⁺], Calcd. for C₅₂H₇₂O₄ 783.9; Anal. Calcd. for C₅₂H₇₂O₄: C, 82.06; H, 9.53. Found: C, 81.61; H, 9.58.

5,11,17,23-Tetrabromo-25,26,27,28-tetrakis(n-hexyloxy)calix[4]arene-1,3-alternate (22). N-Bromosuccinimide (3.0 g, 17 mmol) was added to a suspension of calix[4]arene 21 (2.0 g, 2.6 mmol) in acetone (500 mL), and the mixture was stirred at rt for 48 h exposed to the laboratory light. The thus formed solid was isolated by filtration, washed with acetone (2 x 100 mL) and used in the next step without further purification. (1.5 g, 53%): ¹H NMR δ 7.12 (s, 8 H), 3.56 (s, 8 H), 3.52 (t, J = 7.5 Hz, 8 H), 1.6-1.4 (m, 8 H), 1.4-1.3 (m, 24 H), 0.93 (t, J = 6.9 Hz, 12 H).

5,11,17,23-Tetrahydroxy-25,26,27,28-tetrakis(n-hexyloxy)calix[4]arene-1,3-alternate (23). To a solution of tetrabromo derivative 22 (0.90 g, 0.83 mmol) in freshly
distilled from Na and oxygen-free THF (150 mL) was added \( n\)-BuLi (30 mL of 2M solution in pentane, 60 mmol) at -78 °C, and the mixture was stirred at this temperature for 75 min. Trimethyl borate (14 mL, 145 mmol) was then added at -78 °C, and the mixture was allowed to warm to rt. After 5 h, the reaction mixture was cooled down again to -78 °C, and \( \text{H}_2\text{O}_2 \) (15 mL of 30% aq solution) and NaOH (35 mL of 3N aq solution) was added. The resulting solution was stirred overnight at rt, after which the precipitate was filtered. The mother liquor was cooled to 0 °C and treated with NaS\textsubscript{2}O\textsubscript{3} (25 g), after which the mixture was filtered and the filtrate was concentrated in vacuo. The residue was treated with 5% aq HCl (100 mL), and the colorless precipitate was filtered and washed with MeOH (50 mL) afforded 23 (0.27 g, 40%). mp = 230 - 232 °C. \( ^1\text{H} \text{NMR} \left( \text{DMSO-}\text{d}_6 \right) \delta \ 8.39 \text{ (bs, 4 H), 6.34 (s, 8 H), 3.50 (s, 8 H), 3.02 (t, } J = 7.5 \text{ Hz, 8 H), 1.3-1.25 (m, 8 H), 1.25-1.1 (m, 16 H), 1.1-1.0 (m, 8 H), 0.87 (t, } J = 7.5 \text{ Hz, 12 H); MALDI-TOF MS m/z 847 ([M+Na\textsuperscript{+}], Calcd for C\textsubscript{52}H\textsubscript{72}O\textsubscript{8} 847.5, 11,17,23,25,26,27,28-Octa(\( n\)-hexyloxy)calix[4]arene-\( 1,3\)-alternate \( (24). \) To a suspension of 23 (0.30 g, 0.36 mmol) and NaH (0.15 g of 60% (wt.) suspension in mineral oil, 3.6 mmol) in freshly distilled DMF (50 mL) was added \( n\)-hexylbromide (0.46 mL, 3.2 mmol), and the reaction mixture was stirred at 70 °C under nitrogen for 24 h. The precipitate was filtered off, and the mother liquor was treated with a mixture of crushed ice (50 g), water (50 mL) and CH\textsubscript{2}Cl\textsubscript{2} (100 mL). The organic layer was separated, washed with water (2 x 100 mL), dried over MgSO\textsubscript{4} and evaporated. The residue was recrystallized from 10:1 MeOH-CHCl\textsubscript{3} to yield calix[4]arene 24 (0.35 g,
85%). mp = 109 - 112 °C. \(^1\)H NMR δ 6.55 (s, 8 H), 3.83 (t, \(J = 7.5\) Hz, 8 H), 3.62 (s, 8 H), 3.34 (t, \(J = 7.5\) Hz, 8 H), 1.73 (m, 16 H), 1.4-1.2 (m, 48 H), 0.89 (t, \(J = 7.5\) Hz, 24 H); \(^{13}\)C NMR δ 153.6, 150.7, 134.4, 115.2, 71.6, 68.1, 37.8, 32.3, 31.8, 29.8, 26.0, 25.9, 22.9, 22.7, 14.3, 14.1; MALDI-TOF MS m/z 1182 ([M+Na\(^+\)], Calcd for C\(_{76}\)H\(_{120}\)O\(_8\)Na 1183.

**General procedure for alklylation of 25,26,27,28-Tetrahydroxycalix[4] arenes.**

**Preparation of 1,3-Alternates:** To a suspension of tetrahydroxycalix[4]arene (0.01 mol) and K\(_2\)CO\(_3\) (4.2 g, 0.03 mol) in MeCN (200 mL) an alkyl bromide (0.03 mol) was added, and the reaction mixture was refluxed under nitrogen for 48 h. The precipitate was filtered off, and the solution was evaporated to dryness. The residue was redissolved in CH\(_2\)Cl\(_2\) (200 mL), and the solution was washed with water (3 x 150 mL) and dried over MgSO\(_4\). After evaporation, the solid residue was treated with MeOH (200 mL) to yield the corresponding 25,27-bis(alkyloxy)-26,28-hydroxycalix[4]arene as white solid. To a suspension of this compound (0.01 mol) and Cs\(_2\)CO\(_3\) (50 g, 0.15 mol) in MeCN (300 mL) an alkylbromide (0.04 mol) was added, and the reaction mixture was refluxed under nitrogen for 48 h. After cooling, the precipitate was filtered off and treated with a mixture of water (100 mL) and CH\(_2\)Cl\(_2\) (100 mL). The organic layer was separated, washed with water (2 x 100 mL), dried over MgSO\(_4\), and solvent was evaporated to afford white solid.
25,27-Hydroxy-26,28-bis(n-hexyloxy)-p-tert-butylcalix[4]arene (25). (76%). $^1$H NMR δ 7.82 (s, 2 H), 7.03 (s, 4 H), 6.84 (s, 4 H), 4.28 (d, $J = 13.5$ Hz, 4 H), 3.96 (t, $J = 6.0$ Hz, 4 H), 3.29 (d, $J = 13.5$ Hz, 4 H), 2.01 (m, 4 H), 1.66 (m, 4 H), 1.40 (m, 8 H), 1.26 (s, 18 H), 1.00 (s, 18 H), 0.92 (t, $J = 7.5$, 6 H).

25,27-Hydroxy-26,28-bis(n-propyloxy)-p-tert-butylcalix[4]arene (26). (81%). $^1$H NMR δ 7.86 (s, 2 H), 7.02 (s, 4 H), 6.83 (s, 4 H), 4.28 (d, $J = 12.5$ Hz, 4 H), 3.92 (t, $J = 6.5$ Hz, 4 H), 3.28 (d, $J = 12.5$ Hz, 4 H), 2.01 (m, 4 H), 1.31 (m, 4 H), 1.25 (s, 18 H), 0.99 (s, 18 H), 0.82 (m, 3 H). These data are in agreement with previously published data.$^{80}$

25,26,27,28-Tetrakis(n-hexyloxy)-p-tert-butylcalix[4]arene-1,3-alternate (27). (42%). mp 231-233 °C; $^1$H NMR δ 6.95 (s, 8 H), 3.73 (s, 8 H), 3.38 (t, $J = 7.5$ Hz, 8 H), 1.28 (s, 36 H), 1.25-1.1 (m, 32 H), 0.86 (t, $J = 7.5$ Hz, 12 H); $^{13}$C NMR δ 154.8, 143.4, 133.1, 126.0, 70.8, 39.0, 33.9, 32.0, 31.8, 31.7, 29.7, 25.6, 23.0, 14.2; MALDI-TOF m/z 985.71 ([M + H]$^+$; Calcd for C$_{68}$H$_{105}$O$_4$, 985.80), 1007.93 ([M + Na]$^+$; Calcd for C$_{68}$H$_{104}$O$_4$Na, 1007.78).

25,26,27,28-Tetrakis(n-propyloxy)-p-tert-butylcalix[4]arene-1,3-alternate (28). (49%). $^1$H NMR δ 6.95 (s, 8 H), 3.80 (s, 8 H), 3.29 (t, $J = 7.4$ Hz, 8 H), 1.25 (s, 36 H), 0.97 (m, 8 H), 0.60 (t, $J = 7.5$ Hz, 12 H). These data are in agreement with previously published data.$^{64}$

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Preparation of calix[4]arene- NO\(^+\) complexes


Stock solutions of NO\(_2\)/N\(_2\)O\(_4\) were freshly prepared upon slowly injected of NO\(_2\)/N\(_2\)O\(_4\) into CHCl\(_3\) in a sealed vial, The gas concentration was determined gravimetrically. In a typical procedure, solution of calix[4]arene 18 (50 mg, 0.065 mmol) in dry, freshly distilled 5.0 mL CHCl\(_3\) was mixed with the stock solution of NO\(_2\)/N\(_2\)O\(_4\) (~3 eq) in CHCl\(_3\) and SnCl\(_4\) (1.5 eq) at rt. After 1 h, complex 29 was precipitated upon addition of hexane, filtered off, washed with hexane (2 x 5 mL), and dried in \textit{vacuo} (77 mg, 90%).

Procedure 2. Calix[4]arene- NO\(^+\) complexes were obtained upon mixing 18 (50 mg, 0.065 mmol) with an excess NO\(^+\)SbF\(_6\)^\(-\) (26 mg, 0.10 mmol) in dry CHCl\(_3\). Complex 18•NO\(^+\)SbF\(_6\)^\(-\) formed within 20 h. The UV-vis, FTIR and \(^1\)H NMR spectra are identical with the respective complex 29 (65 mg, 97%).

\(^1\)H NMR \(\delta\) 6.99 (s, 8 H), 4.39 (d, \(J = 12.5\) Hz, 4 H), 4.02 (t, \(J = 7.5\) Hz, 8 H), 3.44 (d, \(J = 12.5\) Hz, 4 H), 2.0-1.9 (m, 8 H), 1.5-1.3 (m, 24 H), 0.93 (t, \(J = 7.5\) Hz, 12 H); UV-vis (CHCl\(_3\) \(\lambda_{\text{max}}\) nm) 563; FTIR (CDCl\(_3\) \(\nu\) cm\(^{-1}\)) 1923 (NO\(^+\)), 1461, 1298, 1047 (NO\(_3\)^\(-\)).

5,11,17,23-Tetranitro-25,26,27,28-tetra-\textit{n}-hexyloxy calix[4]arene (30). Excess NO\(_2\) (20 eq) react with 18 (50 mg, 0.05 mmol) to generate 30 in quantitative yield overnight. Recrystallization from MeOH afford 30 as white crystals. (45 mg, 95%) mp 166-167\(^\circ\)C.

\(^1\)H NMR \(\delta\) 7.56 (s, 8 H), 4.50 (d, \(J = 12.5\), 4 H), 3.97 (t, \(J = 7.5\) Hz, 8 H), 3.39 (d, \(J =
12.5 Hz, 8 H), 1.87 (m, 8 H), 1.36 (br s, 24 H), 0.92 (t, J = 6.5 Hz, 12 H). These data are in agreement with previously published data.63

25,26,27,28-Tetra (n-hexyloxy)calix[4]arene-1,3-alternate - NO⁺ Complex (31). Complex 31 and 21•NO⁺SbF₆⁻ were obtained analogously as dark blue solid. (> 90%);

¹H NMR δ 7.17 (t, J = 7.5 Hz, 4 H), 7.08 (d, J = 7.5 Hz, 8 H), 3.87 (t, J = 7.5 Hz, 8 H), 3.60 (s, 8 H), 1.9-1.8 (m, 8 H), 1.4-1.3 (m, 24 H), 0.93 (t, J = 7.5 Hz, 12 H); UV-vis (CHCl₃, λmax, nm) 524; FTIR (CDCl₃ ν cm⁻¹) 1955 (NO⁺), 1438, 1246, 1091 (NO₃⁻);

Anal. Calcd. for C₁₅₂H₂₄O₂•NO⁺NO₃⁻•1.5SnCl₄: C, 50.21; N, 2.25; H, 5.83. Found: C, 50.23; N, 1.82; H, 5.99.

Tetrakis(O-n-hexyloxy)cyclophane (34). NaH (0.11 g of 60% suspension in mineral oil, 2.70 mmol) was added to the solution of Pappalardo’s cyclophane (0.20 g, 0.34 mmol) in freshly distilled DMF (20 mL), and the mixture was stirred under nitrogen for 30 min. n-Hexylbromide (0.30 mL, 2.04 mmol) was then added, and the reaction mixture was stirred at 70 °C for 3 days. The precipitate was collected and dissolved in CH₂Cl₂ (20 mL). The solution was washed with water (3 x 20 mL), dried over MgSO₄ and evaporated. The residue was recrystallized from MeOH-CHCl₃ to afford 34 as a white powder (0.16 g 50%): ¹H NMR δ 3.89 (s, 8 H), 3.58 (t, J = 7 Hz, 8 H), 2.30 (s, 24 H), 1.8-1.7 (m, 8 H), 1.6-1.5 (m, 16 H), 1.4-1.35 (m, 8 H), 1.07 (s, 12 H), 0.91 (t, J = 7 Hz, 12 H); ¹³C NMR δ 153.9, 138.4, 131.4, 126.7, 73.2, 32.8, 32.0, 30.4, 26.0, 22.8,
17.7, 14.2, 13.7; Anal. Calcd for C_{64}H_{96}O_4: C 82.70; H 10.41. Found: C, 82.37; H, 10.25.

25,26,27,28-Tetrakis(n-hexyloxy)-p-tert-butyldcalix[4]arene-1,3-alternate-NO^+ complex (35). Procedure 1. NO_2/N_2O_4 gas was bubbled for 20 sec through the solution of calix[4]arene 27 (25 mg, 0.025 mmol) and SnCl_4 (3 mL, 0.026 mmol) in dry CHCl_3 (0.5-1.0 mL). The solvent was evaporated under the steam of dry nitrogen. The dark-blue precipitate was dissolved in dry CHCl_3 (0.5-1.0 mL) and used for further reactions. Procedure 2. Stock solution of NO_2/N_2O_4 (~3 eq) in CHCl_3 was added to the solution of 2 (1 eq) and SnCl_4 (1.5 eq) in CHCl_3 at rt. After 1 h, complex 1 was precipitated upon addition of hexanes, filtered, washed with hexanes (2 X ), and dried in vacuo (>95%). (Mp can not obtained because it decompose) ^1H NMR δ 7.02 (s, 8 H), 3.77 (t, J = 7.5 Hz, 8 H), 3.60 (s, 8 H), 1.38 (m, 8 H), 1.38 (m, 24 H), 1.30 (s, 36 H), 0.92 (t, J = 7.5 Hz, 12 H); UV-vis (CDCl_3, λ_max, nm) 578; FTIR (CDCl_3 v cm^{-1}) 1934 (NO^+). Anal. Calcd for C_{68}H_{104}Cl_4N_2O_8Sn: C, 61.04; H, 7.83; N, 2.09. Found: C, 60.96; H, 7.88; N, 2.09.

5,11,17,23-Tetranitro-25,26,27,28-tetra-n-propyloxycalix[4]arene-1,3-alternate (38). Excess NO_2 react with 28 generate 38 in quantitative yield overnight. Recrystalization from MeOH afford white crystals. (98%). mp > 280 °C. ^1H NMR δ 7.95 (s, 8 H), 3.79 (t, J = 7.4 Hz, 8 H), 3.73 (s, 8 H), 1.87 (m, 8 H), 1.04 (t, J = 6.5 Hz, 12 H).
*5,11,17,23,25,26,27,28-Octa(n-hexyloxy)calix[4]arene-1,3-alternate* - NO⁺ Complex (39). Complex 39 cannot be prepared using this protocol; only dealkylation/oxidation products were detected. For the NMR characterization, complex 39 was generated in the exchange experiment between NO⁺ complex 31 and free calix[4]arene 24. Complex 24•NO⁺SbF₆⁻ formed immediately upon mixing with an excess NO⁺SbF₆⁻ in dry CHCl₃. (90%) ¹H NMR δ 6.54 (s, 8 H), 3.93 (t, 8 H, 7.5 Hz), 3.76 (t, 8 H, 7.5 Hz), 3.44 (s, 8 H), 1.8-1.75 (m, 8 H), 1.9-1.8 (m, 8 H), 1.5-1.2 (m, 48 H), 0.95 (t, 7.5 Hz, 12 H), 0.89 (t, 7.5 Hz, 12 H); UV-vis (CHCl₃ λmax nm) 600; FTIR (CDCl₃ ν cm⁻¹) 1875 (NO⁺).

25-Hydroxy-26,27,28-trihexyloxy-p-tert-butylcalix[4]arene (40). A mixture of 25,26,27,28-tetrahydroxy-p-tert-butylcalix[4]arene (4.0 g, 6.2 mmol), freshly distilled anhydrous DMF (80 mL), Ba(OH)₂•8H₂O (6.8 g, 21.6 mmol), and BaO (6.36 g, 41.5 mmol) was stirred at rt for 15 min. n-Hexylbromide (21 mL, 184 mmol) was added, and the suspension was stirred at rt for another 12 h. The mixture was diluted with water (100 mL), and the product was extracted with CH₂Cl₂ (3 x 100 mL). The organic layer was washed with water (2 x 100 mL), dried over Na₂SO₄ and evaporated under reduced pressure. The residue was recrystallized from MeOH to give pure 40 as a white solid. (3.8 g, 69%). mp 134-136 °C. ¹H NMR δ 7.11 (s, 2 H), 7.03(s, 2 H), 6.51 (d, 2.3 Hz, 2 H), 6.49 (d, 2.3 Hz, 2 H), 5.72 (s, 1 H), 4.36 (d, 12.8 Hz, 2 H), 4.32 (d, 13.2 Hz, 2 H), 3.89 (t, 8.2 Hz, 2 H), 3.78 (t, 8.1 Hz, 4 H), 3.22 (d, 13.2 Hz, 2
H), 3.16 (d, J = 12.4 Hz, 2 H), 2.3-2.2 (m, 2 H), 2.0-1.8 (m, 4 H), 1.4-1.3 (m, 18 H), 1.32 (s, 9 H), 1.31 (s, 9 H), 0.92 (t, J = 7.3 Hz, 3 H), 0.90 (m, 6 H), 0.81 (s, 18 H).

25-[(Ethoxycarbonyl)methoxy]-26,27,28-trihexyloxy-p-tert-butylcalix[4]arene (41). A mixture of calix[4]arene 40 (5.0 g, 5.6 mmol) and Na$_2$CO$_3$ (10.0 g, 94.0 mmol) in CH$_3$CN (150 mL) was refluxed for 15 min, after which ethyl bromoacetate (10 mL, 90 mmol) was added, and the reflux continued for 12 h. The inorganic salts were filtered, and the solvent was evaporated. The residue was dissolved in CH$_2$Cl$_2$ (100 mL) and washed with water (3 x 50 mL). The solvent was evaporated, and the product was recrystallized from MeOH. (4.9 g, 89%). mp 121-123 °C. $^1$H NMR δ 6.91(s, 2 H), 6.90 (s, 2 H), 6.63 (d, J = 2.5 Hz, 2 H), 6.61 (d, J = 2.5 Hz, 2 H), 4.86 (s, 2 H), 4.66 (d, J = 12.5 Hz, 2 H), 4.38 (d, J = 12.5 Hz, 2 H), 4.18 (q, J = 7.3 Hz, 2 H), 3.83 (t, J = 8.2 Hz, 4 H), 3.75 (t, J = 8.2 Hz, 2 H), 3.15 (d, J = 12.5 Hz, 2 H), 3.10 (d, J = 12.5 Hz, 2 H), 2.2-2.1 (m, 2 H), 2.0-1.9 (m, 4 H), 1.4-1.3 (m, 18 H), 1.27 (t, J = 7.3 Hz, 3 H), 1.18 (s, 9 H), 1.17 (s, 9 H), 0.96 (s, 18 H), 0.9-0.8 (m, 9 H).

25-(Carbomethoxy)-26,27,28-trihexyloxy-p-tert-butylcalix[4]arene (42). A mixture of 41 (2.0 g 2.0 mmol), THF-H$_2$O, 5:1 (100 mL) and KOH (1.0 g, 17.8 mmol) was refluxed for 12 h. The pH was adjusted to 4 with aq 2 M HCl. The product was extracted with CH$_2$Cl$_2$ (2 x 50 mL), and the organic layer was dried over Na$_2$SO$_4$ and evaporated to give 42 as a white solid. (1.86 g, 97%). mp 136-137 °C. $^1$H NMR δ 11.30 (s, 1 H), 7.16 (s, 2 H), 7.14 (s, 2 H), 6.59 (d, J = 2.5 Hz, 2 H), 6.49 (d, J = 2.5 Hz, 2 H),
4.67 (s, 2 H), 4.45 (d, \( J = 12.5 \) Hz, 2 H), 4.23 (d, \( J = 12.5 \) Hz, 2 H), 4.08 (t, \( J = 7.3 \) Hz, 2 H), 3.8-3.7 (m, 4H), 3.24 (d, \( J = 12.5 \) Hz, 2 H), 3.16 (d, \( J = 12.5 \) Hz, 2 H), 1.95-1.8 (m, 6 H), 1.45-1.2 (m, 18 H), 1.35 (s, 18 H), 0.90 (t, \( J = 7.3 \) Hz, 9 H), 0.83 (s, 18 H); MALDI-TOF MS, \( m/z \) 959.2 (M\(^+\), Calcd for \( C_{64}H_{94}O_6 \) 960.4). Anal. Calcd for \( C_{64}H_{94}O_6 \): C 80.12; H 9.88. Found: C, 80.27; H, 9.88.

**N-Succinimide Ester of 25-(Carbomethoxy)-26,27,28-trihexyloxy-\( p\)-tert-butylcalix[4]arene (43).** A suspension of 42 (1.00 g, 1.05 mmol), \( N \)-hydroxy succinimide (1.00 g, 8.70 mmol), DCC (0.21 g 1.05 mmol) and DMAP (0.04 g, 0.32 mmol) in THF (50 mL) was stirred at rt for 12 h under nitrogen. After filtration, the solvent was evaporated, and the residue was redissolved in hexane (50 mL) and filtered again. The hexane solution was evaporated and the residue was purified by column chromatography (CH\(_2\)Cl\(_2\)-hexane, 1:1) to afford 43 as a white solid (0.93 g, 83%). mp 75-78 °C. \(^1\)H NMR \( \delta \) 6.95 (s, 2 H), 6.92 (s, 2 H), 6.62 (d, \( J = 2.5 \) Hz, 2 H), 6.56 (d, \( J = 2.5 \) Hz, 2 H), 5.28 (s, 2 H), 4.56 (d, \( J = 13.0 \) Hz, 2 H), 4.41 (d, \( J = 12.5 \) Hz, 2 H), 3.89 (t, \( J = 7.8 \) Hz, 2 H), 3.79 (t, \( J = 7.8 \) Hz, 2 H), 3.75 (t, \( J = 7.3 \) Hz, 2 H), 3.18 (d, \( J = 13.0 \) Hz, 2 H), 3.12 (d, \( J = 12.5 \) Hz, 2 H), 2.82 (s, 4 H), 2.10 (m, 2 H), 1.190 (m, 4 H), 1.45-1.35 (m, 18 H), 1.20 (s, 18 H), 0.93 (s, 18 H), 0.9-0.8 (m, 9 H). Ester 43 appeared to be relatively unstable, it probably undergoes hydrolysis or reaction with other compounds and attempts to obtain the MALDI-TOF and/or CHN analytical data failed.
5,11,17,23-Tetrakis(t-butyl)-25,26,27-trihydroxy-28-(n-propyloxy)calix[4]arene (44). In the modified procedure, to the solution of t-butyl calix[4]arene (10.0 g, 15.4 mmol) in MeCN (300 mL), K$_2$CO$_3$ (1.07 g, 7.71 mmol) was added. The mixture was refluxed for 15 min, and then n-propyl bromide (14.0 mL, 154.1 mmol) was added. The mixture was further refluxed for 24 h, and the solvent was evaporated under reduced pressure. The residue was taken up with CH$_2$Cl$_2$ (200 mL), washed with 1M HCl (2 x 200 mL) and H$_2$O (200 mL), and dried over MgSO$_4$. The solvent was evaporated, and the residual solid was recrystallized from CHCl$_3$/CH$_3$OH to afford product 44 as white crystals (6.28 g, 59%). $^1$H NMR $\delta$ 10.20 (s, 1 H), 9.61 (s, 2 H), 7.06 (m, 8 H), 4.37 (d, $J$ = 12.5 Hz, 2 H), 4.27 (d, $J$ = 12.5 Hz, 2 H), 4.10 (t, $J$ = 7.5 Hz, 2 H), 3.44 (d, $J$ = 12.5 Hz, 2 H), 3.42 (d, $J$ = 12.5 Hz, 2 H), 2.18 (m, 2 H), 1.24 (t, $J$ = 7.5 Hz, 3 H), 1.21 (s, 9 H), 1.19 (s, 27 H) $^{13}$C NMR $\delta$ 151.5, 148.6, 148.1, 147.9, 143.7, 128.5, 128.3, 127.8, 126.5, 125.8, 78.9, 34.3, 34.1, 34.0, 33.3, 32.5, 31.6, 31.4, 31.3, 25.4, 23.3, 22.8, 14.2, 10.8. The spectral data are in agreement with the previously published.$^{80}$

5,11,17,23-Tetrakis(t-butyl)-25-allyloxy-26,28-dihydroxy-27-(n-propyloxy)calix[4]arene (45). To a solution of calix[4]arene 44 (4.0 g, 5.8 mmol) in MeCN (150 mL), K$_2$CO$_3$ (3.2 g, 23.2 mmol) was added, and the mixture was refluxed under nitrogen for 15 min. Allyl bromide (9.5 mL, 10.6 mmol) was then added, and the mixture was further refluxed for 24 h. The solvent was evaporated under reduced pressure, the residue was redissolved in CH$_2$Cl$_2$ (100 mL), washed with 1M HCl (2 x 50 mL), H$_2$O (50 mL), and dried over MgSO$_4$. The solvent was evaporated, and the residual solid was
recrystallized from CHCl₃/CH₃OH to afford 45 as white crystals (2.8g 67%). mp 187-190 °C. ¹H NMR δ 7.64 (s, 2 H), 7.03 (s, 4 H), 6.83 (s, 2 H) 6.82 (s, 2 H), 6.23 (m, 1 H), 5.75 (d, J = 17.4 Hz, 1 H), 5.36 (d, J = 12.5 Hz, 1 H), 4.52 (d, J = 7.0 Hz, 2 H), 4.30 (d, J = 12.5 Hz, 2 H), 4.28 (d, J = 12.5 Hz, 2 H), 3.95 (t, J = 7.5 Hz, 2 H), 3.29 (d, J = 12.5 Hz, 4 H), 2.02 (m, 2 H), 1.27 (s, 18 H), 1.24 (t, J = 7.5 Hz, 3 H), 0.98 (s, 18 H); ¹³C NMR δ 150.8, 150.0, 149.9, 146.9, 146.8, 141.4, 133.2, 132.9, 127.9, 127.8, 125.6, 125.5, 125.1, 117.5, 33.9, 31.9, 31.8, 31.2, 23.5, 11.0; FTIR (KBr ν cm⁻¹): ν = 3413, 2961, 2904, 1643, 1486, 1361, 1196; Anal. Calcd. for C₅₀H₆₆O₄: C, 82.15; H, 9.10. Found: C 81.82, H 9.34; MALDI-FTMS, m/z: 753.4837 [(M+Na)⁺, Calcd. for C₅₀H₆₆O₄ 753.4853].

5,11,17,23-Tetrakis(t-butyl)-25-allyloxy-26,27,28-tris-(n-propyloxy)calix[4]arene, 1,3-alternate (46). To the solution of calix[4]arene 45 (5.0 g, 6.8 mmol) in MeCN (400 mL), Cs₂CO₃ (17.8 g, 54.7 mmol) was added, and the mixture was refluxed under nitrogen for 15 min. n-Propyl bromide (6.2 mL, 68.4 mmol) was then added, and the mixture was further refluxed for 36 h. The solvent was evaporated under reduced pressure. The residue was redissolved in CH₂Cl₂ (100 mL), washed with 1M HCl (2 x 50 mL), H₂O (50 mL), and dried over MgSO₄. The solvent was evaporated to afford calix[4]arene 46 as white crystals (3.9 g 70%). mp 243-245 °C. ¹H NMR δ 6.97 (s, 2 H), 6.95 (s, 2 H), 6.94 (d, J = 2.5 Hz, 2 H), 6.92 (d, J = 2.5 Hz, 2 H), 5.38 (m, 1 H), 4.76 (m, 1 H), 4.72 (s, 1 H), 3.79 (s, 4 H), 3.78 (s, 4 H), 3.71 (m, 2 H), 3.33 (m, 6 H), 1.26 (s, 18 H), 1.22 (s, 18 H), 1.08 (m, 6 H), 0.66 (t, J = 7.5 Hz, 9 H); ¹³C NMR δ 154.9, 154.7,
5,11,17,23-Tetrakis(t-butyl)-25-(3'-hydroxypropyloxy)-26,27,28-tris-(n-propyloxy)-calix[4]arene, 1,3-alternate (47). Solution of BH$_3$•THF in THF (1.0 M, 36 mL) was added dropwise to a stirred solution of compound 46 (3.0 g, 3.7 mmol) in dry THF (200 mL) at -10 °C under nitrogen. The reaction mixture was stirred for 1 h while warming to rt, then stirred for another 2.5 h. 1M aq NaOH (20 mL) was added dropwise over 10 min, followed by H$_2$O$_2$ (30%, 11 mL) and H$_2$O (2 mL). The mixture was stirred at rt for 1 h and then at 40 °C for 12 h. Brine was added, and the organic layer was separated. The aqueous layer was extracted with THF (2 x 20 mL), and the combined organic solution was washed with brine (3 x 30 mL) and dried over MgSO$_4$. The solvent was evaporated, and the residue was crystallized from CHCl$_3$/CH$_3$OH to afford product 47 as white crystals (2.9 g 95%). mp > 275 °C. $^1$H NMR δ 7.00 (d, $J = 2.5$ Hz, 2 H), 6.98 (m, 4 H), 6.95 (s, 2 H), 3.82 (m, 8 H), 3.32 (m, 10 H), 1.39 (m, 2 H), 1.26 (s, 18 H), 1.24 (s, 18 H), 1.03 (m, 2 H), 0.92 (m, 4 H) 0.61 (m, 9 H); $^{13}$C NMR δ 154.9, 154.6, 143.9, 143.8, 133.5, 133.3, 132.9, 126.1, 126.0, 125.8, 125.5; 1199, 1012; FTIR (KBr ν cm$^{-1}$) 3468, 2955, 2935, 2923, 2863, 1594, 1475, 1199, 1012; Anal. Calcd for
Calix[4]arene Siloxane (48). To a solution of calix[4]arene 46 (0.50 g, 0.61 mmol) in dry toluene, the Karstedt catalyst (Pt₂{[(CH₂=CH)Me₂Si]₂O}₃, 0.50 mL, 3% Pt in xylene) was added dropwise at 40 °C under nitrogen, and the mixture was stirred for 1 h, after which SiH(OEt)₃ (0.70 mL, 0.92 mmol) was added dropwise, and the resulting mixture was heated at 90 °C for another 24 h. The solvent was evaporated, and the product 48 was purified by column chromatography to afford white crystals 48 (0.24 g, 40%). ¹H NMR δ 6.99 (s, 1 H), 6.98 (s, 1 H), 6.95 (s, 2 H), 6.93 (s, 4 H), 3.8 (m, 8 H), 3.75 (m, 6 H), 3.36 (m, 6 H), 3.24 (t, J = 7.6 Hz, 3H), 1.47 (m, 2 H), 1.26 (s, 18 H), 1.24 (s, 18 H), 1.21 (t, J = 7.0 Hz, 9 H), 1.14 (m, 4 H), 0.98 (m, 2 H), 0.67 (t, J = 7.5 Hz, 6 H), 0.58 (t, J = 7.5 Hz, 3 H), 0.43 (m, 2 H); ¹³C NMR δ 155.1, 154.9, 154.7, 143.5, 143.4, 143.1, 133.2, 133.0, 126.3, 125.9, 125.8, 73.6, 72.1, 71.7, 58.5, 58.4, 39.2, 39.0, 33.9, 31.7, 31.5, 30.4, 23.2, 22.7, 22.3, 18.4, 10.2, 10.1, 6.4; FTIR (KBr, ν, cm⁻¹): 2962, 2901, 2873, 2029, 1597, 1482, 1473, 1360, 1243, 1211, 1123; MS ESI TOF, m/z 979.6829 ([M+H⁺], Calcd for C₆₂H₉₄O₇Si 979.6841).

Calix[4]arene Functionalized Silica Gel (49). A suspension of ester 43 (100 mg, 95 mmol), 3-aminopropyl-functionalized silica gel (Aldrich) (226 mg, 155 mmol) and Et₃N (92.9 mg, 0.92 mmol) in THF (50 mL) was stirred at rt for 12 h. The solid was filtered, washed with CH₂Cl₂, MeOH, water, MeCN, and THF, and then dried under reduced
pressure at 100 °C for 3 days. Affording 49 as white powder (220 mg, 0.117 meq/g). FTIR (KBr ν cm⁻¹): 3383, 2960, 1650, 1556, 1477. Anal. Found for 3-aminopropyl silica gel (0.687 meq/g, C₉H₂₃NO₃Si): C, 7.42; H, 1.80; N, 1.91. Anal. Calcd for silica gel 49 (17% loading, 0.117 meq/g, C₇₃H₁₁₅NO₈Si): C, 15.43; H, 2.68; N, 1.82. Found: C 15.34; H 2.97; N, 1.70.

25-[(n-Octylcarbamoylmethoxy)-26,27,28-trihexyloxy-p-tert-butylcalix[4]arene (50). To the solution of ester 43 (75.0 mg, 0.07 mmol) in THF (10 mL), n-octylamine (18 mg, 0.14 mmol) and Et₃N (70 mg, 0.7 mmol) were added, and the reaction mixture was stirred at rt for 12 h. The precipitate was filtered, and the solution was evaporated. The residue was redissolved in CH₂Cl₂ (20 mL), washed with 2 M aq HCl (2 x 5 mL) and water (5 mL), and dried over Na₂SO₄. The organic layer was then evaporated and the residue was recrystallized from CH₃CN to afford 50 as a white solid (48 mg, 65%); ¹H NMR δ 8.43 (t, J = 6.2 Hz, 1 H), 6.99 (s, 2 H), 6.97 (s, 2 H), 6.57 (s, 4 H), 4.71 (s, 2 H), 4.38 (d, J = 13.0 Hz, 2 H), 4.35 (d, J = 13.0 Hz, 2 H), 3.9-3.7 (2 x m, 6 H), 3.42 (dt, J = 9.5 Hz, J = 6.2 Hz, 2 H), 3.23 (d, J = 13.3 Hz, 2 H), 3.14 (d, J = 12.8 Hz, 2 H), 2.0-1.8 (3 x m, 8 H), 1.5-1.3 (m, 30 H), 1.25 (s, 9 H), 1.23 (s, 9 H), 0.93 (s, 18 H), 0.95-0.85 (m, 12 H). FTIR (KBr ν cm⁻¹): 3346 (NH), 2964, 1680 (C=O), 1537, 1473. Anal. Calcd for C₇₂H₁₁₁NO₅•0.5CH₃CN: C, 80.35; H, 10.39; N, 1.93. Found: C 80.02; H 10.09; N, 1.91. Compound 50 was also independently synthesized from the acid chloride of 42 (prepared with SOCl₂), n-octylamine and Et₃N in CHCl₃.
Silica gel Supported Calix[4]arene (51). The suspension of silica gel (150 Å pore size, 5 g) and 18% aq HCl (20 mL) was refluxed for 9 h, after which the mixture was filtered and washed with deionized water until pH ~ 4. The thus activated silica gel was dried under vacuum (0.1 mm Hg) at 100 °C for 48 h. The mixture of calix[4]arene 48 (0.7 g, 0.7 mmol) and the activated silica gel (2.3 g) in CH₂Cl₂ was stirred at room temperature for 48 h and then filtered. The filtrate was washed successively with CH₂Cl₂, acetone, water, THF, and ether to afford silica gel supported material 50 as a white powder (2.2 g, ~ 9.5 loading weight). FTIR (KBr ν cm⁻¹): 2965, 2357, 1633, 1470, 1106, 966, 801, 471. Anal. Cald. for 9.5% loading C, 7.82; H, 0.94. Found: C, 7.49; H, 1.34; TGA: 10% weight lost.

Poly(ethylene glycol) methyl ether methanesulfonate (Polymer 54). Poly(ethylene glycol) methyl ether (10.0 g, MW 5000, 2.0 mmol) was dissolved in dry CH₂Cl₂ (100 mL). The solution was cooled to 0 °C, and then Et₃N (0.54 mL, 4.00 mmol) and methanesulfonyl chloride (0.5 mL, 4.0 mmol) were added sequentially. The reaction mixture was stirred at 0 - 5 °C for 2 h, washed with water (2 x 40 mL) and treated with brine (40 mL). The organic layer was separated and dried with MgSO₄, and the solvent was evaporated in vacuo. The residue was washed with hexanes to afford product 53 (10.0 g, 98%): ¹H NMR δ 3.65 (m, 513 H), 3.36 (s, 3 H), 3.07 (s, 3 H).

Poly(ethylene glycol) methylether calix[4]arene (Polymer 55). To the solution of calix[4]arene 47 (1.0 g, 1.2 mmol) in dry THF (100 mL) potassium tert-butoxide (0.81
g, 7.2 mmol) was added under nitrogen, and the resulting mixture was stirred at 50 °C for 20 min. After cooling to rt, polymer 53 (3.00 g, 0.59 mmol) in dry THF (100 mL) was added dropwise, and the mixture was stirred at 50 °C for 60 h. The solvent was evaporated; the residue was redissolved in CH₂Cl₂ (50 mL), washed with water (2 x 20 mL), brine (20 mL), and dried over MgSO₄. The solvent was evaporated under reduced pressure, and the residual solid was washed thoroughly with diethyl ether to remove unreacted calix[4]arene (TLC control). The resulting product 55 was air dried and then dried in vacuo for 12 h to afford 55 (0.8 g). ¹H NMR δ 6.96 (m, 4.39 H), 3.36 (s, 3 H), 1.24 (m, 21.7 H), 0.97 (m), 0.59 (m); Calcd. loading is 55%. FTIR (KBr, ν cm⁻¹): 2948, 2885, 2741, 2695, 2238, 1967, 1468, 1414, 1360, 1343, 1281, 1242, 1149, 1110, 1060, 962, 947, 842, 529.

**Preparation of Amides (57a-q).** Amides 57a-q were synthesized by standard procedures upon mixing equimolar amounts of the corresponding amines and acid chlorides (0.5 g) in H₂O-EtOAc, 1:1 in the presence of K₂CO₃, and purified by recrystallization from MeOH afford amides at 30 - 70% yields. ¹H NMR (CDCl₃). Physical properties were previously reported.

**N-Methyl-propionamide (57a).** ¹H NMR δ 6.12 (bs, 1 H), 2.77 (bs, 3 H), 2.26 (q, J = 7.5 Hz, 2 H), 1.11 (t, J = 7.5 Hz, 3 H).
**N-Methyl-butyramide (57b).** $^1$H NMR $\delta$ 5.74 (bs, 1 H), 2.77 (d, $J = 4.5$ Hz, 3 H), 2.12 (t, $J = 7.5$ Hz, 2 H), 1.59-1.66 (m, 2 H), 0.91 (t, $J = 7.5$ Hz, 3 H).$^{90c}$

**N-Methyl-pentanamide (57c).** $^1$H NMR $\delta$ 6.43 (bs, 1 H), 2.69 (d, $J = 4.5$ Hz, 3 H), 2.09 (t, $J = 7.5$ Hz, 2 H), 1.48-1.54 (m, 2 H), 1.22-1.28 (m, 2 H), 0.81 (t, $J = 7.5$ Hz, 3 H).

**N-Methyl-hexanamide (57d).** $^1$H NMR $\delta$ 6.24 (bs, 1 H), 2.71 (d, $J = 4.5$ Hz, 3 H), 2.10 (t, $J = 7.5$ Hz, 2 H), 1.51-1.58 (m, 2 H), 1.22-1.28 (m, 4 H), 0.81 (t, $J = 7.5$ Hz, 3 H).

**N-Methyl-octanamide (57e).** $^1$H NMR $\delta$ 5.41 (bs, 1 H), 2.79 (d, $J = 4.5$ Hz, 3 H), 2.13 (t, $J = 7.5$ Hz, 2 H), 1.53-1.58 (m, 2 H), 1.22-1.28 (m, 8 H), 0.85 (t, $J = 7.5$ Hz, 3 H).

**N-Methyl-pivalamide (57f).** $^1$H NMR $\delta$ 5.69 (bs, 1 H), 2.78 (d, $J = 4.5$ Hz, 3 H), 1.15 (s, 9 H).

**N-Ethyl-propionamide (57g).** $^1$H NMR $\delta$ 5.56 (bs, 1 H), 3.26 (m, 2 H), 2.17 (q, $J = 7.5$ Hz, 2 H), 1.16 (t, $J = 7.5$ Hz, 3 H), 1.13 (t, $J = 7.5$ Hz, 3 H).

**N-Ethyl-butyramide (57h).** $^1$H NMR $\delta$ 5.52 (bs, 1 H), 3.22-3.16 (m, 2 H), 2.07 (t, $J = 7.5$ Hz, 2 H), 1.53-1.60 (m, 2 H), 1.06 (t, $J = 7.5$ Hz, 3 H), 0.86 (t, $J = 7.5$ Hz, 3 H).
\textbf{N-Ethyl-valeramide (57i).} $^1$H NMR $\delta$ 5.96 (bs, 1 H), 3.21 (m, 2 H), 2.10 (t, $J = 7.5$ Hz, 2 H), 1.53 (m, 2 H), 1.28 (m, 2 H), 1.07 (t, $J = 7.5$ Hz, 3 H), 0.85 (t, $J = 7.5$ Hz, 3 H).$^{102}$

\textbf{N-Ethyl-hexanamide (57j).} $^1$H NMR $\delta$ 5.95 (bs, 1 H), 3.14 (m, 2 H), 2.11 (t, $J = 7.5$ Hz, 2 H), 1.56 (m, 2 H), 1.45 (m, 2 H), 1.24 (m, 2 H), 0.87 (t, $J = 7.5$ Hz, 3 H), 0.84 (t, $J = 7.5$ Hz, 3 H).

\textbf{N-Propyl-propionamide (57k).} $^1$H NMR $\delta$ 5.85 (bs, 1 H), 3.15 (m, 2 H), 2.15 (q, $J = 7.5$ Hz, 2 H), 1.47 (m, 2 H), 1.10 (t, $J = 7.5$ Hz, 3 H), 0.86 (t, $J = 7.5$ Hz, 3 H).

\textbf{N-Propyl-butiramide (57l).} $^1$H NMR $\delta$ 5.52 (bs, 1 H), 3.19 (q, $J = 7.5$ Hz, 2 H), 2.14 (t, $J = 7.5$ Hz, 2 H), 1.61-1.68 (m, 2 H), 1.46-1.55 (m, 2 H), 0.95 (t, $J = 7.5$ Hz, 3 H), 0.92 (t, $J = 7.5$ Hz, 3 H).

\textbf{N-Propyl-valeramide (57m).} $^1$H NMR $\delta$ 5.64 (bs, 1 H), 3.17 (q, $J = 7.5$ Hz, 2 H), 2.14 (t, $J = 7.5$ Hz, 2 H), 1.58 (m, 2 H), 1.49 (m, 2 H), 1.32 (m, 2 H), 0.91 (t, $J = 7.5$ Hz, 6 H), 0.87 (t, $J = 7.5$ Hz, 6 H).

\textbf{N-Propyl-hexanamide (57n).} $^1$H NMR $\delta$ 6.04 (bs, 1 H), 3.14 (q, $J = 7.5$ Hz, 2 H), 2.10 (t, $J = 7.5$ Hz, 2 H), 1.56 (m, 4 H), 1.45 (m, 4 H), 1.24 (m, 2 H), 0.86 (t, $J = 7.5$ Hz, 3 H), 0.81 (t, $J = 7.5$ Hz, 3 H).
**N-i-Propyl-valeramide (57o).** $^1$H NMR δ 5.46 (bs, 1 H), 3.98-4.09 (m, 1 H), 2.09 (t, $J$ = 7.5 Hz, 2 H), 1.53-1.59 (m, 2 H), 1.26-1.34 (m, 2 H), 1.10 (d, $J$ = 7.5 Hz, 6 H), 0.87 (t, $J$ = 7.5 Hz, 3 H).

**N-α-Butyl-pivalamide (57p).** $^1$H NMR δ 5.39 (bs, 1 H), 1.36 (s, 9 H), 1.14 (s, 9 H).

**N-Benzyl-butyramide (57q).** $^1$H NMR δ 7.32-7.28 (m, 2 H), 7.26-7.24 (m, 3 H), 5.96 (bs, 1 H), 4.41 (d, $J$ = 6.5 Hz, 2 H), 2.17 (t, $J$ = 7.5 Hz, 2 H), 1.62-1.70 (m, 2 H), 0.93 (t, $J$ = 7.5 Hz, 3 H).

**General Nitrosation Procedure with Encapsulated Reagent 35.** Calix[4]arene - NO$^+$ complex 35 (1 eq) was added to the solution of amide 57a-q (1-3 eq) in freshly distilled CHCl$_3$, and the reaction mixture was stirred at rt for 5 h. The solvent was evaporated, and the residue was analyzed by $^1$H NMR spectroscopy and in some cases separated by preparative TLC, resulting in $N$-nitrosoamides as orange oils. All runs were performed at least in duplicate. The spectral data for the obtained $N$-nitroso compounds 58a-e were identical with those independently obtained from 57a-e and NO$_2$/N$_2$O$_4$ in CHCl$_3$ (yields $>$ 95%) following the literature protocols$^{103,104}$ The corresponding $^1$H NMR spectra are attached below. $N$-nitrosoamides 58f-q cannot be obtained from 57f-q and complex 35. All these $N$-nitrosoamides are oily liquids except stated specifically.
N-Methyl-N-nitroso-propionamide (58a). 102 (50%); $^1$H NMR $\delta$ 3.14 (q, $J = 7.5$ Hz, 2 H) 3.05 (s, 3 H), 1.26 (t, $J = 7.5$ Hz, 3 H).

N-Methyl-N-nitroso-butyramid (58b). (68%); $^1$H NMR $\delta$ 3.09 (t, $J = 7.5$ Hz, 2 H), 3.05 (s, 3 H), 1.76-1.81 (m, 2 H), 0.97 (t, $J = 7.5$ Hz, 3 H).90c

N-Methyl-N-nitroso-valeramide (58c). (53%); $^1$H NMR $\delta$ 3.17 (t, $J = 7.5$ Hz, 2 H), 3.10 (s, 3 H), 1.75-1.81 (m, 2 H), 1.40-1.47 (m, 2 H), 0.95 (t, $J = 7.5$ Hz, 3 H).102

N-Methyl-N-nitroso-hexamidine (58d). 105 (95%); $^1$H NMR $\delta$ 3.13 (t, $J = 7.5$ Hz, 2 H), 3.08 (s, 3 H), 1.75-1.81 (m, 2 H), 1.32-1.36 (m, 4 H), 0.88 (t, $J = 7.5$ Hz, 3 H).

N-Methyl-N-nitroso-octynamidine (58e).105 (63%); $^1$H NMR $\delta$ 3.19 (t, $J = 7.5$ Hz, 2 H), 3.12 (s, 3 H), 1.72-1.81 (m, 2 H), 1.26-1.41 (m, 8 H), 0.86 (t, $J = 7.5$ Hz, 3 H).

N-Ethyl-N-nitroso-propionamide (58g).106 $^1$H NMR $\delta$ 3.76 (q, $J = 7.5$ Hz, 2 H), 3.12 (q, $J = 7.5$ Hz, 2 H), 1.26 (t, $J = 7.5$ Hz, 3 H), 0.92 (t, $J = 7.5$ Hz, 3 H).

N-Ethyl-N-nitroso-butyramid (58h).107 $^1$H NMR $\delta$ 3.80 (q, $J = 7.5$ Hz, 2 H), 3.14 (t, $J = 7.5$ Hz, 2 H), 1.79-1.85 (m, 2 H), 1.03 (t, $J = 7.5$ Hz, 3 H), 0.97 (t, $J = 7.5$ Hz, 3 H); $^{13}$C NMR $\delta$ 178.4, 36.7, 34.1, 18.6, 13.8, 12.0.
\textbf{N-Propyl-N-nitroso-propionamide (58k).}^{108} \textsuperscript{1}H NMR \(\delta\) 3.72 (t, \(J = 7.5\) Hz, 2 H), 3.16 (q, \(J = 7.5\) Hz, 2 H), 1.53-1.60 (m, 2 H), 1.20 (t, \(J = 7.5\) Hz, 3 H), 0.94 (t, \(J = 7.5\) Hz, 3 H); \textsuperscript{13}C NMR \(\delta\) 178.9, 40.3, 28.5, 22.4, 20.4, 11.6.

\textbf{N-Propyl-N-nitroso-butyramide (58l).} \textsuperscript{1}H NMR \(\delta\) 3.72 (t, \(J = 7.5\) Hz, 2 H), 3.14 (t, \(J = 7.5\) Hz, 2 H), 1.79-1.86 (m, 2 H), 1.34-1.41 (m, 2 H), 1.03 (t, \(J = 7.5\) Hz, 3 H), 0.81 (t, \(J = 7.5\) Hz, 3 H); \textsuperscript{13}C NMR \(\delta\) 178.8, 40.1, 36.6, 20.4, 18.7, 13.6, 11.2.

\textbf{N-Propyl-N-nitroso-valeramide (58m).} \textsuperscript{1}H NMR \(\delta\) 3.72 (t, \(J = 7.5\) Hz, 2 H), 3.16 (t, \(J = 7.5\) Hz, 2 H), 1.74-1.79 (m, 2 H), 1.41-1.46 (m, 2 H), 1.34-1.40 (m, 2 H), 0.95 (t, \(J = 7.5\) Hz, 3 H) 0.81 (t, \(J = 7.5\) Hz, 3 H); \textsuperscript{13}C NMR \(\delta\) 178.8, 40.3, 34.6, 27.2, 22.4, 20.3, 13.8, 11.4.

\textbf{N-Benzyl-N-nitroso-butyramide (58q).}^{107} \textsuperscript{1}H NMR \(\delta\) 7.24-7.27 (m, 3 H), 7.16-7.17 (m, 2 H), 4.92 (s, 2 H), 3.19 (t, \(J = 7.5\) Hz, 2 H), 1.80-1.87 (m, 2 H), 1.02 (t, \(J = 7.5\) Hz, 3 H).

61 and 62 are synthesized following the standard procedure with NO\textsubscript{2} and SnCl\textsubscript{4}.

5,11,17,23-Tetra-\(\tau\)-butyl-25,27-bis(n-hexyloxy)-26,28-bis[\(\text{(S)}\)-(+)2-methylbutyloxy]calix[4]arene, \textit{1,3-alternate} (61). (42\%). mp 142-145 °C. \textsuperscript{1}H NMR \(\delta\) 6.95 (s, 4 H), 6.94 (s, 4 H), 3.75 (m, 8 H), 3.35 (m, 4 H), 3.26 (t, \(J = 7.0\) Hz, 4 H), 1.53 (m, 2 H), 1.28 (s, 18 H), 1.25 (s, 18 H), 1.21 (m, 8 H), 1.11 (m, 8 H), 1.03 (d, \(J = 5.0\) Hz), 0.97 (d, \(J = 5.5\) Hz), 0.94 (d, \(J = 7.5\) Hz), 0.88 (d, \(J = 7.5\) Hz), 0.80 (d, \(J = 7.5\) Hz), 0.76 (d, \(J = 7.5\) Hz), 0.74 (d, \(J = 7.5\) Hz), 0.72 (d, \(J = 7.5\) Hz), 0.69 (d, \(J = 7.5\) Hz), 0.66 (d, \(J = 7.5\) Hz), 0.63 (d, \(J = 7.5\) Hz), 0.61 (d, \(J = 7.5\) Hz), 0.59 (d, \(J = 7.5\) Hz), 0.57 (d, \(J = 7.5\) Hz), 0.55 (d, \(J = 7.5\) Hz), 0.53 (d, \(J = 7.5\) Hz), 0.51 (d, \(J = 7.5\) Hz), 0.49 (d, \(J = 7.5\) Hz), 0.47 (d, \(J = 7.5\) Hz), 0.45 (d, \(J = 7.5\) Hz), 0.43 (d, \(J = 7.5\) Hz), 0.41 (d, \(J = 7.5\) Hz), 0.39 (d, \(J = 7.5\) Hz), 0.37 (d, \(J = 7.5\) Hz), 0.35 (d, \(J = 7.5\) Hz), 0.33 (d, \(J = 7.5\) Hz), 0.31 (d, \(J = 7.5\) Hz), 0.29 (d, \(J = 7.5\) Hz), 0.27 (d, \(J = 7.5\) Hz), 0.25 (d, \(J = 7.5\) Hz), 0.23 (d, \(J = 7.5\) Hz), 0.21 (d, \(J = 7.5\) Hz), 0.19 (d, \(J = 7.5\) Hz), 0.17 (d, \(J = 7.5\) Hz), 0.15 (d, \(J = 7.5\) Hz), 0.13 (d, \(J = 7.5\) Hz), 0.11 (d, \(J = 7.5\) Hz), 0.09 (d, \(J = 7.5\) Hz), 0.07 (d, \(J = 7.5\) Hz), 0.05 (d, \(J = 7.5\) Hz), 0.03 (d, \(J = 7.5\) Hz), 0.01 (d, \(J = 7.5\) Hz).
Hz, 4 H), 0.86 (t, J = 7.0 Hz, 6 H), 0.81 (t, J = 7.5 Hz, 6 H), 0.48 (d, J = 6.5 Hz, 6 H);
$^{13}$C NMR δ 155.6, 155.1, 143.2, 143.1, 133.3, 133.0, 132.8, 132.7, 126.4, 126.2, 126.1,
126.0, 76.8, 70.8, 39.3, 39.2, 34.9, 34.0, 33.9, 32.1, 31.8, 31.7, 29.1, 26.5, 25.7, 23.2,
17.3, 14.2, 11.3; MALDI-MS, m/z 979.7481 ([M+Na$^+$], calcd for C$_{66}$H$_{100}$O$_4$Na
979.7519); $[\alpha]_D = 3.92$ (c = 5.0, CHCl$_3$).

1,3-alternate (62) (15%). mp 251-252 °C. $^1$H NMR δ 6.97 (s, 4 H), 6.95 (s, 4 H), 3.72
(m, 8 H), 3.28 (m, 8 H), 1.64 (m, 4 H), 1.26 (bs, 36 H), 1.03 (d, J = 5.0 Hz, 8 H), 0.84
(t, J = 8.0 Hz, 12 H), 0.57 (d, J = 7.0 Hz, 12 H); $^{13}$C NMR δ 155.9, 142.6, 132.6, 132.6,
127.0, 126.9, 77.5, 34.9, 33.9, 31.7, 26.7, 17.3, 11.3; MALDI-FTMS, m/z 951.7235
([M+Na$^+$], calcd for C$_{64}$H$_{96}$O$_4$Na 951.7235; $[\alpha]_D = 5.36$ (c = 2.7, CHCl$_3$).

NO$_2$/N$_2$O$_4$ gas was bubbled for 20 sec through the solution of calix[4]arene (1 x 10$^{-5}$
 mol) and SnCl$_4$ (~2.5 x 10$^{-5}$ mol) in dry CHCl$_3$ (1 mL). The solvent was evaporated
under the stream of dry nitrogen. The dark-colored precipitate was redissolved in dry
CH$_2$Cl$_2$ (1 mL) and used for further reactions. Yields 90-95%.

Complex (63). $^1$H NMR δ 7.06 (s, 4 H), 7.02 (s, 4 H), 3.75 (t, J = 8.0 Hz, 4 H), 3.58 (m,
12 H), 1.96 (m, 2 H), 1.83 (m, 4 H), 1.30 (m, 20 H), 1.33 (s, 18 H), 1.26 (s, 18 H), 1.07
Complex (64). $^1$H NMR $\delta$ 7.06 (s, 8 H), 3.88 (m, 4 H), 3.62 (m, 8 H), 3.53 (m, 4 H), 1.96 (m, 4 H), 1.83 (m, 4 H), 1.28 (m, 20 H), 1.23 (s, 18 H), 1.07 (d, $J = 6.5$ Hz, 12 H), 0.99 (t, $J = 7.0$ Hz, 12 H); UV-vis (CDCl$_3$, $\lambda_{\text{max}}$, nm): 590; FTIR (CDCl$_3$, $\nu$, cm$^{-1}$): 1934 (NO$^+$).

(R,S)-N-Methyl-(3-methyl)valeramide ((R,S)-65). Amides 65 were synthesized by the standard procedures upon mixing equimolar amounts of the corresponding amines and acid chlorides in H$_2$O-EtOAc, 1:1 in the presence of K$_2$CO$_3$, and purified by recrystallization from MeOH (50%); $^1$H NMR (C$_6$D$_6$) $\delta$ 4.29 (bs, 1 H), 2.42 (d, $J = 4.5$ Hz, 3 H), 1.96 (m, 1 H), 1.82 (dd, $J = 14.5$ Hz, $J = 6.0$ Hz, 1 H), 1.55 (dd, $J = 14.5$ Hz, $J = 6.0$ Hz, 1 H), 1.30 (m, 1 H), 1.10 (m, 1 H), 0.87 (d, $J = 7.0$ Hz, 3 H), 0.82 (t, $J = 7.5$ Hz, 3 H); $^{13}$C NMR $\delta$ 173.8, 44.0, 32.3, 29.5, 26.2, 19.2, 11.4; El-MS, $m/z$ 129.0 [M$^+$], calcd for C$_7$H$_{17}$NO 129.1.

N-Methyl-(S)-3-methylvaleramide ((S)-65). The mixture of (S)-3-Methylpentanoic acid$^{109}$ (2 mL, ) and SOCl$_2$ (15 mL) was refluxed for 4 h. Excess SOCl$_2$ was evaporated in vacuum and the resulting acid chloride was redissolved in CH$_2$Cl$_2$ (10 mL). This solution was added dropwise to a mixture of methylamine and Et$_3$N in CH$_2$Cl$_2$ (10 mL) at ~0 °C. The resulting mixture was stirred at rt for 2 h, and then acidified with 10% aq
HCl, washed with water (3 x 15 mL), dried over MgSO₄, and solvent was evaporated under reduced pressure. (90%, ee > 95%, NMR, Pirkle’s reagent). \(^1\)H NMR (\(\text{C}_6\text{D}_6\)) \(\delta\) 4.29 (bs, 1 H), 2.42 (d, \(J = 4.5\) Hz, 3 H), 1.96 (m, 1 H), 1.82 (dd, \(J = 14.5\) Hz, \(J = 6.0\) Hz, 1 H), 1.55 (dd, \(J = 14.5\) Hz, \(J = 6.0\) Hz, 1 H), 1.29 (m, 1 H), 1.09 (m, 1 H), 0.87 (d, \(J = 7.0\) Hz, 3 H), 0.82 (t, \(J = 7.5\) Hz, 3 H).

**Nitrosation with Chiral Reagents (63, 64).** The standard nitrosation procedure applied, after which the reaction mixture was evaporated under reduced pressure at rt. The residual oil was separated by column chromatography with hexanes-\(\text{CH}_2\text{Cl}_2\), 2:1 for 63 and hexanes-\(\text{C}_6\text{H}_6\), 3:1 for 64. Fractions containing \(N\)-nitroso-(2-methyl)valeramides 66 were collected and evaporated under reduced pressure at rt. The resulting oil was treated with TFA (20-25 mL) at rt for 14 h, after which the volatiles were evaporated to give pure \(N\)-methyl-2-methyl)valeramides 65 in 40-50% yield.

**(\(R,S\))-\(N\)-Methyl-\(N\)-nitroso-(3-methyl)valeramide ((\(R,S\))-66).** (Oily liquid) \(^1\)H NMR \(\delta\) 3.16 (m, 1 H), 3.10 (s, 3 H), 3.0 (m, 1 H), 2.07 (m, 1 H), 1.43 (m, 1 H), 1.30 (m, 1 H), 0.98 (d, \(J = 8.0\) Hz, 3 H), 0.88 (t, \(J = 8.0\) Hz, 3 H); \(^{13}\)C NMR \(\delta\) 177.2, 41.5, 32.1, 29.6, 25.7, 19.8, 11.3; EI-MS, \(m/z\) 158.1 [M⁺], calcd for \(\text{C}_7\text{H}_{14}\text{N}_2\text{O}_2\) 158.1.

**\(N\)-Ethyl-octanamide (67a).** (Liquid) \(^1\)H NMR \(\delta\) 5.41 (bs, 1 H), 3.24-3.32 (m, 2 H), 2.13 (t, \(J = 7.5\) Hz, 2 H), 1.59 (m, 2 H), 1.27 (m, 8 H), 1.12 (t, \(J = 7.5\) Hz, 3H), 0.68 (t, \(J = 7.5\) Hz, 3 H).
\textit{N-Propyl-octanamide (67b).} (liquid). $^1\text{H}$ NMR $\delta$ 5.42 (bs, 1 H), 3.21 ($q$, $J = 6.0$, 2 H), 2.15 ($t$, $J = 7.5$ Hz, 2 H), 1.63 (m, 2 H), 1.52 (m, 2 H), 1.20-1.34 (m, 8 H), 0.92 ($t$, $J = 7.5$ Hz, 3 H), 0.86 ($t$, $J = 7.5$ Hz, 3 H).

\textbf{Nitrosation Procedure with Silica Gel Supported Reagent (51).} The suspension of material 50 in dry CH$_2$Cl$_2$ NO$_2$/N$_2$O$_4$ was bubbled for ~10 sec. The dark-blue colored solid was filtered off and washed with CH$_2$Cl$_2$ and suspended in CH$_2$Cl$_2$. The corresponding amide (1:1) was added the mixture and stirred at room temperature for 20 h. After filtration, the solvent was evaporated and the residue was analyzed by $^1\text{H}$ NMR spectroscopy in CDCl$_3$.

\textbf{Nitrosation Procedure with PEG Supported Reagent (56).} NO$_2$/N$_2$O$_4$ was bubbled through the solution of polymer 55 (1 g, 0.17 mmol calix[4]arene) in dry CH$_2$Cl$_2$ (10 mL) for 2-3 min, after which N$_2$ was bubbled through the solution for 10-15 min. The resulting dark solution was divided into three equal parts. \textit{N-methyl octanamide 57e} (5.4 mg, 0.034 mmol), \textit{N-ethyl octanamide 67a} (5.9 mg, 0.034 mmol), and \textit{N-propyl octanamide 67b} (6.3 mg, 0.034 mmol) were separately added to each solution, and the reaction mixtures were kept at rt for 2-3 h. The solvent was evaporated at rt under reduced pressure. Hexanes (10 mL) were added, and the mixture was stirred for 10 min, followed by filtration of the recovered polymer. The solvent was evaporated at rt under reduced pressure, and the residue was dried for 3 h in \textit{vacuo}. The product yield was determined by $^1\text{H}$ NMR spectroscopy.
N-Ethyl-N-nitroso-octanamide (68a). $^1$H NMR $\delta$ 3.80 (q, $J = 7.5$ Hz, 2 H), 3.12 (t, $J = 7.5$ Hz, 2 H), 1.75-1.82 (m, 2 H), 1.26-1.41 (m, 8 H), 0.96 (t, $J = 7.5$ Hz, 3 H), 0.87 (t, $J = 7.5$ Hz, 3 H).

N-Propyl-N-nitroso-octanamide (68b). $^1$H NMR $\delta$ 3.72 (t, $J = 7.5$ Hz, 2 H), 3.13 (t, $J = 7.5$ Hz, 2 H), 1.75-1.82 (m, 2 H), 1.36-1.42 (m, 2 H), 1.26-1.41 (m, 8 H), 0.87 (t, $J = 7.5$ Hz, 3 H) 0.81 (t, $J = 7.5$ Hz, 3 H).
APPENDIX 1

$^1$H NMR SPECTRA OF
(CARBONYL)(MESO-TETRA-$P$-
TOLYLPORPHYRINATO) RU(II) [RU(TTP)(CO)] (14)
ACQUISITION PARAMETERS

File Name = Proton_RuTTP_CO_Chlor
Author =
Sample ID = S054737
Content = Single Pulse Experiment
Creation Date = 20-NOV-2002 13:33:08
Revision Date = 24-APR-2004 01:25:48
Spec Site = Eclipse+ 500
Spec Type = DELTA_NMR
Data Format = 1D COMPLEX
Dimensions = X
Dim Title = 1H
Dim Size = 32768
Dim Units = [ppm]
Field_strength = 11.7473579[tesla] (500[MHz])
X_acq_duration = 3.637248[s]
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 32768
X_resolution = 0.27493314[Hz]
X_sweep = 9.00900901[kHz]
Mod_return = 1
Scans = 24
X_90_width = 15[us]
X_acq_time = 3.637248[s]
X_angle = 45[deg]
X_pulse = 7.5[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Relaxation_delay = 4[s]
Unblank_time = 2[us]
ACQUISITION PARAMETERS

File Name          = Proton_RuTTP_CO_Chlor
Author             =
Sample ID          = S#354797
Content            = Single Pulse Experiment
Creation Date      = 20-NOV-2002 13:33:08
Revision Date      = 24-APR-2004 01:25:48
Spec Site          = Eclipse+ 500
Spec Type          = DELTA NMR
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Dim Units          = ppm
Field_strength     = 11.7473579 [T] (500 [MHz])
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X_domain           = 1H
X_freq             = 500.15991521 [MHz]
X_offset           = 5 [ppm]
X_points           = 32768
X_prescans         = 0
X_resolution       = 0.23493514 [Hz]
X_90_width         = 15 [us]
X_acq_time         = 3.637248 [s]
X_angle            = 45 [deg]
X_pulse            = 7.5 [us]
Initial_wait       = 1 [s]
Phase_preset       = 0 [us]
Relaxation_delay   = 4 [s]
Unblank_time       = 2 [us]
APPENDIX 2

$^1$H NMR SPECTRA OF
NITRATO(NITROSYL)(MESO-TETRA-P-
TOLYL)PORPHYRINATO)RU(II) [RU(TTP)(NO)(ONO$_2$)] (15)
--- ACQUISITION PARAMETERS ---

File Name = Proton_RuTTP_NO2_Colu
Author =
Sample ID = S#751341
Content = Single Pulse Experiment
Creation Date = 14-MAR-2003 01:42:47
Revision Date = 28-APR-2004 01:21:31
Spec Site = Eclipse+ 500
Spec Type = DELTA NMR
Dimensions = X
Dim Title = 1H
Dim Size = 16384
Dim Units = [ppm]
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X_acq_duration = 2.1823488 [s]
X_domain = 1H
X_freq = 500.15991521 [MHz]
X_offset = 5 [ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189 [Hz]
X_sweep = 7.50750751 [kHz]
Scans = 9

X_90_width = 15 [us]
X_acq_time = 2.1823488 [s]
X_angle = 45 [deg]
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Initial_wait = 1 [s]
Phase_preset = 3 [us]
Relaxation_delay = 4 [s]
Unblank_time = 2 [us]
--- ACQUISITION PARAMETERS ---

File Name = Proton_RuTTP_NO2_Colu
Author =
Sample ID = S#751341
Content = Single Pulse Experiment
Creation Date = 14-MAR-2003 01:42:47
Revision Date = 28-APR-2004 01:21:31
Spec Site = Eclipse+ 500
Spec Type = DELTA_NMR
Data Format = 1D COMPLEX
Dimensions = X
Dim Title = 1H
Dim Size = 16384
Dim Units = [ppm]
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X_acq_duration = 2.1823488[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Mod_return = 1
Scans = 1
X_90_width = 15[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 7.5[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Relaxation_delay = 4[s]
Unblank_time = 2[us]
APPENDIX 3

$^1$H NMR SPECTRA OF

25,26,27,28-TETRAKIS(N-HEXYLOXY)-CALIXARENE (18)
APPENDIX 4

$^1$H NMR SPECTRA OF
25,26,27,28-TETRA(N-HEXYLOXY)
CALIX[4]ARENE-1,3-ALTERNATE (21)
APPENDIX 5

$^1$H NMR SPECTRA OF
5,11,17,23-TETRABROMO-25,26,27,28-
TETRAKIS(N-HEXYLOXY)CALIX[4]ARENE-1,3-ALTERNATE (22)
Filename         = 0315tetrbrs 2.jdf
Experiment       = single_pulse.exp
Sample_id        = S#423823
Solvent          = CHLOROFORM D
Creation_time    = 15 MAR 2002 12:50:03
Revision_time    = 23 NOV 2005 04:04:28
Current_time     = 23 NOV 2005 04:05:00
Content          = Single Pulse Experiment
Data format      = 1D COMPLEX
Dim_size         = 16384
Dim_title        = 1H
Dim_units        = [ppm]
Dimensions       = X
Site             = Eclipse+ 500
Spectrometer     = DELTA_NMR
Field_strength   = 11.7473579[T] (500[MHz])
X_acq_duration   = 2.1823488[s]
X_freq           = 500.15991521[MHz]
X_offset         = 5[ppm]
X_points         = 16384
X_acq_time       = 2.1823488[s]
X_90_width       = 15[us]
X_angle          = 45[deg]
X_pulse          = 7.5[us]
Initial_wait     = 1[s]
Phase_preset     = 3[us]
Recvr_gain       = 19
Relaxation_delay = 4[s]
Temp_get         = 22.8[dC]
Unbl ank_time    = 2[us]
APPENDIX 6

$^1$H NMR SPECTRA OF
5,11,17,23,25,26,27,28-OCTA
(N-HEXYLOXY)CALIX[4]ARENE-1,3-ALTERNATE (24)
APPENDIX 7

$^1$H NMR SPECTRA OF
25,27-HYDROXY-26,28-
APPENDIX 8

$^1$H NMR SPECTRA OF
25,27-HYDROXY-26,28-
BIS($N$-PROPYLOXY)-$P$-TERT-BUTYL CALIX[4]ARENE (26)
APPENDIX 9

$^1$H NMR SPECTRA OF
25,26,27,28-TETRAKIS(N-HEXYLOXY)-
P-TERT-BUTYLCALIX[4]ARENE-1,3-ALTERNATE (27)
abundance

X : parts per Million : 1H

Filename = 10094tbu4hx13 5.jdf
Experiment = Single_pulse.exp
Sample id = S#566263
Solvent = CHLOROFORM D
Creation time = 9 OCT 2003 16:51:51
Revision time = 23 NOV 2005 03:34:29
Current time = 23 NOV 2005 03:36:55

Content = Single Pulse Experime
Data format = 1D COMPLEX
Dim size = 16384
Dim title = 1H
Dim units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA NMR
Field_strength = 11.7473579 [T] (500 [MHz])
X_acq_duration = 2.1823488 [s]
X_freq = 500.15991521 [MHz]
X_offset = 5 [ppm]
X_points = 16384
X_resolution = 0.45822189 [Hz]
X_acq_time = 2.1823488 [s]
X_sweep = 7.50750751 [kHz]
X_90_width = 15 [us]
X_angle = 45 [deg]
X_pulse = 7.5 [us]
Initial_wait = 1 [s]
Phase_preset = 3 [us]
Recvr_gain = 12
Relaxation_delay = 4 [s]
Temp.get = 22.4 [°C]
Unblank_time = 2 [us]

R = Hex
APPENDIX 10

$^{1}$H NMR SPECTRA OF
25,26,27,28-TETRAKIS(N-PROPYLOXY)-
$P$-TERT-BUTYLCALIX[4]ARENE-1,3-ALTERNATE (28)
Filename = Proton_4PrCalix_13Alt
Experiment = single_pulse.exp
Sample_id = 4PrClx
Solvent = CHLOROFORM D
Creation time = 28 JAN 2004 15:48:53
Revision time = 23 NOV 2005 04:44:42
Current time = 23 NOV 2005 04:44:59
Content = Single Pulse Experiment
Data format = 1D COMPLEX
Dim size = 16384
Dim title = 1H
Dim units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA NMR
Field_strength = 11.7473579[T] (500[MHz])
X_duration = 2.1823488[s]
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Mod_return = 1
Scans = 24
X_90_width = 15[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 7.5[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 33
Relaxation_delay = 2[s]
Temp_set = 22.2[degC]
Unblank_time = 2[us]

X : parts per Million : 1H
APPENDIX 11

$^1$H NMR SPECTRA OF
5,11,17,23-TETRANITRO-25,26,27,28-
TETRA-$N$-HEXYLOXYCALIX[4]ARENE (30)
Filename = 0805steve4nitro-3.jdf
Experiment = single_pulse.exp
Sample_id = S#336040
Solvent = CHLOROFORM D
Creation_time = 5 AUG 2002 11:51:00
Revision_time = 20Nov 2005 03:34:22
Current_time = 20 Nov 2005 03:37:12

Content = Single Pulse Experiment
Data format = 1D COMPLEX
Dim size = 16384
Dim title = 1H
Dim units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA NMR
Field_strength = 11.7473579[T] (500[MHz])
X_acq_duration = 2.1823488[s]
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Mod_return = 1
Scans = 11
X_90_width = 15[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pul se = 7.5[us]
Initial_wait = 1[s]
Phase_preset = 2[us]
Recvr_gain = 15
Relaxation_delay = 4[s]
Temp_get = 24.1[dC]
Unblark_time = 2[us]

X : parts per Million : 1H

[Diagram of chemical structure]
APPENDIX 12

$^1$H NMR SPECTRA OF
25,26,27,28-TETRAKIS(N-HEXYLOXY)-
$P$-TERT-BUTYLCALIX[4]ARENE-1,3-ALTERNATE-NO$^+$ COMPLEX (35)
X : parts per Million : 1H
APPENDIX 13

\(^1\)H NMR SPECTRA OF
25,26,27,28-TETRAKIS(N-PROPYLOXY)-
P-TERT-BUTYLCALIX[4]ARENE-1,3-ALTERNATE-NO\(^+\) COMPLEX (36)
APPENDIX 14

$^1$H NMR SPECTRA OF
25-HYDROXY-26,27,28-TRIHEXYLOXY-
$P$-TERT-BUTYLCALIX[4]ARENE (40)
ACQUISITION PARAMETERS

Derived from: Proton_1H3HexCalix_Cone.2
File Name: Proton_1H3HexCalix_Cone
Author: S#41527
Sample ID: S#414527
Content: Single Pulse Experiment
Creation Date: 13-DEC-2002 14:57:27
Revision Date: 22-APR-2004 00:22:46
Spec Site: Eclipse+ 500
Spec Type: DELTA NMR
Data Format: 1D COMPLEX
Dimensions: X
Dim Title: 1H
Dim Size: 16384
Dim Units: [ppm]
Field_strength: 11.7473579 [T] (500 [MHz])
X_acq_duration: 2.1823488 [s]
X_domain: 1H
X_freq: 500.15991521 [MHz]
X_offset: 5 [ppm]
X_points: 16384
X_resolution: 0.45822189 [Hz]
X_sweep: 7.50750751 [kHz]
Mod_return: 1
Scans: 24
X_90_width: 15 [us]
X_acq_time: 2.1823488 [s]
X_angle: 45 [deg]
X_pulse: 7.5 [us]
Initial_wait: 1 [s]
Phase_preset: 3 [us]
Relaxation_delay: 4 [s]
Unblank_time: 2 [us]

X: parts per Million: 1H
1H NMR spectrum of a compound showing signal peaks at various ppm values. The spectrum includes details such as field strength, X acquisition duration, X freq, and X offset.

**ACQUISITION PARAMETERS**

- **File Name**: Proton_1H3HexCalix_Co
- **Author**:
- **Sample ID**: S#414527
- **Content**: Single Pulse Experiment
- **Creation Date**: 13-OCT-2002 14:57:27
- **Revision Date**: 22-APR-2004 00:22:46
- **Spec Site**: Eclipse+ 500
- **Spec Type**: DELTA_NMR
- **Data Format**: 1D COMPLEX
- **Dimensions**: X
- **Dim Title**: 1H
- **Dim Size**: 16384
- **Dim Units**: [ppm]
- **Field_strength**: 11.7473579 [T] (500 [MHz])
- **X_acq_duration**: 2.1823488 [s]
- **X_domain**: 1H
- **X_freq**: 500.15991521 [MHz]
- **X_offset**: 5 [ppm]
- **X_points**: 16384
- **X_resolution**: 0.45822189 [Hz]
- **X_sweep**: 7.50750751 [kHz]
- **Mod_return**: 1
- **Scans**: 24
- **X_90_width**: 15 [us]
- **X_acq_time**: 2.1823488 [s]
- **X_angle**: 45 [deg]
- **X_pulse**: 7.5 [us]
- **Initial_wait**: 1 [s]
- **Phase_preset**: 3 [us]
- **Relaxation_delay**: 4 [s]
- **Unblank_time**: 2 [us]
APPENDIX 15

$^1\text{H}$ NMR SPECTRA OF
25-[(ETHOXYCARBONYL)METHOXY]-
APPENDIX 16

$^1$H NMR SPECTRA OF
25-(CARBOMETHOXY)-26,27,28-
TRIHEXYLOXY-$P$-TERT-BUTYL CALIX[4]ARENE (42)
--- ACQUISITION PARAMETERS ---

File Name: Proton_3Hex1MonoAcid

Author: 

Sample ID: S#347808

Content: Single Pulse Experiment

Creation Date: 14-OCT-2002 12:56:38

Revision Date: 22-APR-2004 00:36:42

Spec Site: Eclipse+ 500

Spec Type: DELTA NMR

Data Format: 1D COMPLEX

Dimensions: X

Dim Title: 1H

Dim Size: 16384

Dim Units: [ppm]

Field_strength: 11.7473579 [T] (500 [MHz])

X_acq_duration: 2.1823488 [s]

X_domain: 1H

X_freq: 500.15991521 [MHz]

X_offset: 5 [ppm]

X_points: 16384

X_prescans: 0

X_resolution: 0.45822189 [Hz]

X_sweep: 7.50750751 [kHz]

X_90_width: 15 [us]

X_acq_time: 2.1823488 [s]

X_angle: 45 [deg]

X_pulse: 7.5 [us]

Initial_wait: 1 [s]

Phase_preset: 3 [us]

Relaxation_delay: 4 [s]

Unblank_time: 2 [us]
----- ACQUISITION PARAMETERS -----  
File Name = Proton_3Hex1MonoAcid_ 
Author = 
Sample ID = S9347808  
Content = Single Pulse Experiment  
Creation Date = 14-OCT-2002 12:56:38  
Revision Date = 22-APR-2004 00:36:42  
Spec Site = Eclipse+ 500  
Spec Type = DELTA NMR  
Data Format = 1D COMPLEX  
Dimensions = X  
Dim Title = 1H  
Dim Size = 16384  
Dim Units = [ppm]  
Field_strength = 11.7473579[T] (500[MHz])  
X_acq_duration = 2.1823488[s]  
X_domain = 1H  
X_freq = 500.15991521[MHz]  
X_offset = 5[ppm]  
X_points = 16384  
X_resolution = 0.45822189[Hz]  
X_sweep = 7.50750751[kHz]  
X_90_width = 15[us]  
X_acq_time = 2.1823488[s]  
X_angle = 45[deg]  
X_pulse = 7.5[us]  
Initial_wait = 1[s]  
Phase_preset = 3[us]  
Relaxation_delay = 4[s]  
Unblank_time = 2[us]
APPENDIX 17

$^1$H NMR SPECTRA OF
APPENDIX 18

--- ACQUISITION PARAMETERS ---

File Name = Proton_3HPrClx_Cone.2
Author =
Sample ID = S481208
Content = Single Pulse Experiment
Creation Date = 15-AUG-2003 13:58:52
Revision Date = 22-APR-2004 02:02:37
Spec Site = Eclipse+ 500
Spec Type = DELTA NMR
Data Format = 1D COMPLEX
Dimensions = X
Dim Title = 1H
Dim Size = 16384
Dim Units = [ppm]
Field strength = 11.7473579 [T] (500 [MHz])
X_acq_duration = 2.1823488 [s]
X_domain = 1H
X_freq = 500.15991521 [MHz]
X_offset = 5 [ppm]
X_points = 16384
X_resolution = 0.45822189 [Hz]
X_sweep = 7.50750751 [kHz]
Mod_return = 1
Scans = 17
X_90_width = 15 [us]
X_acq_time = 2.1823488 [s]
X_angle = 45 [deg]
X_pulse = 7.5 [us]
Initial_wait = 1 [s]
Phase_preset = 3 [us]
Relaxation_delay = 2 [s]
Unblank_time = 2 [us]
--- ACQUISITION PARAMETERS ---

File Name = C13_3HPrCalix.2
Author =
Sample ID = S9536232
Content = Single Pulse with Bro
Creation Date = 3-JUN-2003 21:54:32
Revision Date = 23-APR-2004 01:34:33
Spec Site = Eclipse+ 500

Spec Type = DELTA_NMR
Data Format = 1D COMPLEX
Dimensions = X
Dim Title = 13C
Dim Size = 65536
Dim Units = [ppm]
Field_strength = 11.7473579[T] (500[MHz])
X_acq_duration = 2.0840448[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.47983613[Hz]
X_sweep = 31.44654088[kHz]
X_90_width = 14[us]
X_acq_time = 2.0840448[s]
X_angle = 30[deg]
X_pulse = 4.66666667[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Relaxation_delay = 1[s]
Unblank_time = 2[us]
APPENDIX 19

$^1$H NMR SPECTRA OF
5,11,17,23-Tetrakis(t-butyl)-25-allyloxy-
26,28-dihydroxy-27-(n-propyloxy)calix[4]-arene (45)
--- ACQUISITION PARAMETERS ---

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<td></td>
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<td>2.1823488[s]</td>
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X : parts per Million : 1H

--- Graph ---

![Graph with peaks at various ppm values]
APPENDIX 20

$^1$H AND $^{13}$C NMR SPECTRA OF  
5,11,17,23-TETRAKIS(T-BUTYL)-25-ALLYLOXY- 
26,27,28-TRIS-(N-PROPYLOXY)CALIX[4]ARENE, $1,3$-ALTERNATE (46)
APPENDIX 21

$^1$H NMR SPECTRA OF
5,11,17,23-TETRAKIS(T-BUTYL)-25-(3'-HYDROXYPROPYLEOXY)-
26,27,28-TRIS-(N-PROPYLEOXY)-CALIX[4]ARENE, 1,3-ALTERNATE (47)
APPENDIX 22

$^1$H NMR SPECTRA OF

CALIX[4]ARENE SILOXANE (48)
--- ACQUISITION PARAMETERS ---

File Name = Proton_3PrMono_TriEth
Author =
Sample ID = S#823335
Content = Single Pulse Experiment
Creation Date = 13-FEB-2004 11:56:17
Revision Date = 24-APR-2004 04:08:39
Spec Site = Eclipse+ 500
Spec Type = DELTA_NMR
Data Format = 1D COMPLEX
Dimensions = X
Dim Title = 1H
Dim Size = 16384
Dim Units = [ppm]
Field_strength = 11.7473579 [T] (500 [MHz])
X_acq_duration = 2.1823488 [s]
X_domain = 1H
X_freq = 500.15991521 [MHz]
X_offset = 5 [ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189 [Hz]
X_sweep = 7.50750751 [kHz]
Mod_return = 1
Scans = 24
X_90_width = 15 [us]
X_acq_time = 2.1823488 [s]
X_angle = 45 [deg]
X_pulse = 7.5 [us]
Initial_wait = 1 [s]
Phase_preset = 3 [us]
Relaxation_delay = 2 [s]
Unblank_time = 2 [us]
APPENDIX 23

$^1$H AND $^{13}$C NMR SPECTRA OF  
APPENDIX 24

$^1$H NMR SPECTRA OF
POLY(ETHYLENE GLYCOL)
METHYL ETHER METHANESULFONATE (POLYMER 54)
### ACQUISITION PARAMETERS

- **File Name**: Proton_PEG-O-Me_2
- **Author**: 
- **Sample ID**: S#512867
- **Content**: Single Pulse Experiment
- **Creation Date**: 8-OCT-2003 15:23:17
- **Revision Date**: 24-APR-2004 12:39:43
- **Spec Site**: Eclipse+ 500
- **Spec Type**: DELTA_NMR
- **Data Format**: 1D COMPLEX
- **Dimensions**: X
- **Dim Title**: 1H
- **Dim Size**: 16384
- **Dim Units**: [ppm]
- **Field_strength**: 11.7473579[T] (500[MHz])
- **X_acq_duration**: 2.1823488[s]
- **X_domain**: 1H
- **X_freq**: 500.15991521[MHz]
- **X_offset**: 5[ppm]
- **X_points**: 16384
- **X_acq_time**: 2.1823488[s]
- **X_angle**: 45[deg]
- **X_pulse**: 7.5[us]
- **X_90_width**: 15[us]
- **Scans**: 24
- **Initial_wait**: 1[s]
- **Phase_preset**: 3[us]
- **Relaxation_delay**: 2[s]
- **Unblank_time**: 2[us]

**Diagram Description**:

The diagram shows a spectroscopic analysis with peaks at various ppm values. The x-axis represents parts per million (ppm) scaled for proton (1H) nuclei. The y-axis indicates the intensity of the signal in arbitrary units. Notable peaks are observed at specific ppm values, indicating the presence of specific chemical shifts in the sample.
APPENDIX 25

$^1$H NMR SPECTRA OF

$N$-METHYL-BUTYRAMIDE (57B)
**Filename** = 0127prnhme 2.jdf

**Experiment** = single pulse.exp

**Sample_id** = S#605597

**Solvent** = CHLOROFORM D

**Creation time** = 29 JAN 2003 21:12:29

**Revision time** = 19 NOV 2005 00:28:42

**Current time** = 19 NOV 2005 00:36:31

**Content** = Single Pulse Experiment

**Data format** = 1D COMPLEX

**Dim size** = 16384

**Dim title** = 1H

**Dim units** = [ppm]

**Dimensions** = X

**Site** = Eclipse+ 500

**Spectrometer** = DELTA NMR

**Field_strength** = 11.7473579[T] (500[MHz])

**X_acq_duration** = 2.1823488[s]

**X_freq** = 500.15991521[MHz]

**X_offset** = 5[ppm]

**X_points** = 16384

**X_acq_time** = 2.1823488[s]

**X_domain** = 1H

**X_freq** = 500.15991521[MHz]

**X_offset** = 5[ppm]

**X_points** = 16384

**X_resolution** = 0.45822189[Hz]

**X_sweep** = 7.50750751[kHz]

**X_90_width** = 15[us]

**X_acq_time** = 2.1823488[s]

**X_angle** = 45[deg]

**X_90_pulse** = 3[us]

**Initial_wait** = 1[s]

**Phase_preset** = 3[us]

**Recvr_gain** = 17

**Relaxation_delay** = 4[s]

**Temp_get** = 22.1[dC]

**Unbl ank_time** = 2[us]
APPENDIX 26

$^1$H NMR SPECTRA OF

N-METHYL-PENTANAMIDE (57C)
X : parts per Million : 1H
APPENDIX 27

$^1$H NMR SPECTRA OF

$N$-METHYL-HEXANAMIDE (57D)
APPENDIX 28

$^1$H NMR SPECTRA OF

$N$-METHYL-OCTANAMIDE (57E))


--- ACQUISITION PARAMETERS ---

File Name = Proton_N-Methyl_Octane
Author =
Sample ID = S997908
Content = Single Pulse Experiment
Creation Date = 20-OCT-2003 11:38:17
Revision Date = 24-APR-2004 03:37:50
Spec Site = Eclipse+ 500
Spec Type = DELTA_NMR
Data Format = 1D COMPLEX
Dimensions = X
Dim Title = 1H
Dim Size = 16384
Dim Units = [ppm]
Field_strength = 11.7473579 [T] (500 [MHz])
X_acq_duration = 2.1823488 [s]
X_domain = 1H
X_freq = 500.15991521 [MHz]
X_offset = 5 [ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189 [Hz]
X_sweep = 7.30750751 [kHz]
Mod_return = 1
Scans = 24
X_90_width = 15 [us]
X_acq_time = 2.1823488 [s]
X_angle = 45 [deg]
X_pulse = 7.5 [us]
Initial_wait = 1 [s]
Phase_preset = 3 [us]
Relaxation_delay = 2 [s]
Unblank_time = 2 [us]
APPENDIX 29

$^1$H NMR SPECTRA OF

$N$-METHYL-PIVALAMIDE (57F))
APPENDIX 30

$^1$H NMR SPECTRA OF

$N$-ETHYL-PROPIONAMIDE (57G)
APPENDIX 31

$^1$H NMR SPECTRA OF

$N$-ETHYL-VALERAMIDE (57I)
Filename = 1213etnhvaler 2.jdf
Experiment = single_pulse.exp
Sample_id = S#647980
Solvent = CHLOROFORM D
Creation time = 13 DEC 2002 21:53:50
Revision time = 19 NOV 2005 01:49:58
Current time = 19 NOV 2005 01:50:37

Content = Single Pulse Experiment
Data_format = 1D COMPLEX
Dim size = 16384
Dim title = 1H
Dim units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR

Field_strength = 11.7473579[T] (500[MHz])
X_acq_duration = 2.1823488[s]
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Mod_return = 1
Scans = 6
X_90_width = 15[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 7.5[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 12
Relaxation_delay = 4[s]
Temp_get = 22.1[degC]
Unbl ank_time = 2[us]

X : parts per Million : 1H
APPENDIX 32

$^1$H NMR SPECTRA OF $N$-PROPYL-PROPIONAMIDE (57K)
APPENDIX 33

\( ^1H \text{ NMR SPECTRA OF} \)

\( N\text{-PROPYL-BUTIRAMIDE (57L)} \)
APPENDIX 34

$^1$H NMR SPECTRA OF

$N$-$T$-BUTYL-PIVALAMIDE (57P)
APPENDIX 35

$^1$H NMR SPECTRA OF

$N$-BENZYL-BUTYRAMIDE (57Q)
APPENDIX 36

$^1$H NMR SPECTRA OF
X : parts per Million : 1H
Filename         = 0428chiral 2.jdf
Experiment       = single_pulse.exp
Sample_id        = S#414713
Solvent          = CHLOROFORM D
Creation_time    = 28 APR 2003 16:52:01
Revision_time    = 24 NOV 2005 03:26:34
Current_time     = 24 NOV 2005 03:30:30
Content          = Single Pulse Experiment
Data_format      = 1D COMPLEX
Dim_size         = 16384
Dim_title        = 1H
Dim_units        = [ppm]
Dimensions       = X
Site             = Eclipse+ 500
Spectrometer     = DELTA_NMR
Field_strength   = 11.7473579[T] (500[MHz])
X_acq_duration   = 2.1823488[s]
X_freq           = 500.15991521[MHz]
X_offset         = 5[ppm]
X_resolution     = 0.45822189[Hz]
X_sweep          = 7.50750751[kHz]
Swept return     = 1
Scans            = 18
X_90_width       = 15[us]
X_acq_time       = 2.068[s]
X_angle          = 45[deg]
X_pulse          = 7.5[us]
Initial_wait     = 1[s]
Phase_preset     = 3[us]
Recvr_gain       = 18[dB]
Relaxation_delay = 4[s]
Temp_get         = 22.4[degC]
Unblk_time       = 2[us]
APPENDIX 37

$^1$H NMR SPECTRA OF
5,11,17,23-ΤΕΤΡΑ-Τ-ΒΥΤΥΛ-25,27-26,28-ΤΕΤΡΑΚΙΣ[(S)-(+)2-
APPENDIX 38

$^1$H NMR SPECTRA OF

$(R,S)$-N-METHYL-(3-METHYL)VALERAMIDE $((R,S)$-65)
APPENDIX 39

$^1$H NMR SPECTRA OF

$(S)$-N-METHYL-(3-METHYL)VALERAMIDE ($(S)$-65)
APPENDIX 40

$^1$H NMR SPECTRA OF

(N-ETHYL-OCTANAMIDE (67A))
ACQUISITION PARAMETERS

File Name          = Proton_N-Ethyl_Octane
Author             =
Sample ID          = S8654131
Content            = Single Pulse Experime
Creation Date      = 22-JAN-2004 12:33:52
Revision Date      = 24-APR-2004 03:47:44
Spec Site          = Eclipse+ 500
Spec Type          = DELTA_NMR
Data Format        = 1D COMPLEX
Dimensions         = X
Dim Title          = 1H
Dim Size           = 16384
Dim Units          = [ppm]
Field_strength     = 21.7073579[T] (500[MHz])
X_acq_duration     = 2.1823488[s]
X_domain           = 1H
X_freq             = 500.15991521[MHz]
X_offset           = 5[ppm]
X_points           = 16384
X_resolution       = 0.45822189[Hz]
X_sweep            = 7.50750751[kHz]
Scans              = 16
Scans              =
X_90_width         = 15[us]
X_acq_time         = 2.1823488[s]
X_angle            = 45[deg]
X_pulse            = 7.5[us]
Initial_wait       = 1[s]
Phase_preset       = 3[us]
Relaxation_delay   = 2[s]
Unblank_time       = 2[us]

X : parts per Million : 1H
**ACQUISITION PARAMETERS**

- **File Name:** Proton_N-Ethyl_Octana
- **Author:**
- **Sample ID:** S#854131
- **Content:** Single Pulse Experiment
- **Creation Date:** 22-JAN-2004 12:33:52
- **Revision Date:** 24-APR-2004 03:47:44
- **Spec Site:** Eclipse+ 500
- **Spec Type:** DELTA_NMR
- **Data Format:** 1D COMPLEX
- **Dimensions:** X
- **Dim Title:** 1H
- **Dim Size:** 16384
- **Dim Units:** [ppm]
- **Field_strength:** 11.7473579 [T] (500 [MHz])
- **X_acq_duration:** 2.1823488 [s]
- **X_domain:** 1H
- **X_freq:** 500.15991521 [MHz]
- **X_offset:** 5 [ppm]
- **X_points:** 16384
- **X_preacq:** 0
- **X_resolution:** 0.45822189 [Hz]
- **X_sweep:** 7.50750751 [kHz]
- **Mod_return:** 1
- **Scans:** 16
- **X_90_width:** 15 [us]
- **X_acq_time:** 2.1823488 [s]
- **X_angle:** 45 [deg]
- **X_pulse:** 7.5 [us]
- **Initial_wait:** 1 [s]
- **Phase_preset:** 3 [us]
- **Relaxation_delay:** 2 [s]
- **Unblank_time:** 2 [us]
APPENDIX 41

$^1$H NMR SPECTRA OF

$(N\text{-PROPYL-OCTANAMIDE (67B)})$
--- ACQUISITION PARAMETERS ---
File Name        = Proton_N-Propyl_Octane
Author           =
Sample ID        = S#859045
Content          = Single Pulse Experiment
Creation Date    = 22-JAN-2004 12:41:26
Revision Date    = 24-APR-2004 03:53:00
Spec Site        = Eclipse+ 500
Spec Type        = DELTA_NMR
Data Format      = 1D COMPLEX
Dimensions       = X
Dim Title        = 1H
Dim Size         = 16384
Dim Units        = [ppm]
Field_strength   = 11.7473579[T] (500[MHz])
X_acq_duration   = 2.1823488[s]
X_domain         = 1H
X_freq           = 500.15991521[MHz]
X_offset         = 5[ppm]
X_points         = 16384
X_prescans       = 0
X_resolution     = 0.45822189[Hz]
X_sweep          = 7.0750751[kHz]
Mod_return       = 1
Scans            = 16
X_90_width       = 15[us]
X_acq_time       = 2.1823488[s]
X_angle          = 45[deg]
X_pulse          = 7.5[us]
Initial_wait     = 1[s]
Phase_preset     = 3[us]
Relaxation_delay = 2[s]
Unblank_time     = 2[us]

--- GRAPHS ---

X : parts per Million : 1H
--- ACQUISITION PARAMETERS ---

File Name = Proton_N-Propyl_Octan
Author =
Sample ID = S859045
Content = Single Pulse Experiment
Creation Date = 22-JAN-2004 12:41:26
Revision Date = 24-APR-2004 03:53:00
Spec Site = Eclipse+ 500
Spec Type = DELTA_NMR
Data Format = 1D COMPLEX
Dimensions = X
Dim Title = 1H
Dim Size = 16384
Dim Units = [ppm]
Field_strength = 11.7473579[T] (500[MHz])
X_acq_duration = 2.1823488[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Mod_return = 1
Scans = 16
X_90_width = 15[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 7.5[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Relaxation_delay = 2[s]
Unblank_time = 2[us]

X: parts per Million : 1H
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Yanlong Kang was born in Shijiazhuang, Hebei Province, P. R. China. He obtained his B. S. in 1990 from Nankai University, Tianjin, China. After several years of working in institutions and industry, he came to the United States of America in 2001 and began his doctoral study at the University of Texas at Arlington. He worked with Professor Dmitry M. Rudkevich in a project entitled “Supramolecular chemistry of nitrogen dioxide”. He obtained his doctorate in 2005.